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THE ESSENTIAL QUALITIES OF AN ANAESTHETIST*

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MANY of you will, doubtless, feel that it is presumptuous for a Surgeon to talk of the "essential qualities of an Anaesthetist"; as egotistical almost as if he declared that yellow roses were more beautiful than red! Therefore, you will agree that all that I can hope to do is to outline what one surgeon desires his partner anaesthetist to be.

Every surgeon has different likes and dislikes, all being prima donnas as you well know; therefore, I should never dare to venture to speak for all of them. However, having been a "quasi" anaesthetist myself, and having served as assistant-anaesthetist overseas for a long period, and having come in contact during my lifetime with many of this breed of cat—good, bad and indifferent—I feel that I can at least enjoy myself at your expense, realizing full well that you will eventually have the last word, as I drift lazily off to sleep at the hands of one or other of you, while you playfully "lick your chops"!

In fact, I think that this is a most interesting problem, and one I am sure which each of you has studied individually because, perhaps, no other branch of medicine has made such fabulous progress in the past fifteen years.

It seems only yesterday that I was training as an interne in the Montreal General Hospital, when all but one of the anaesthetists were nurses, with the exception of those of us who had little or no training at all, but whom the poor, unfortunate patients accepted blissfully, believing that because we were doctors we really must be very superior beings. Any of you who can remember those days, when screaming children came to the Out-Door to have their tonsils removed in the morning, and we attempted to induce them with large amounts of open ether and still more physical force, must be encouraged indeed to see the immense progress that has been made.

I should like to quote here from one of the most famous English surgeons of today, Sir Heneage Ogilvie:

> The most notable advance in the period I am reviewing, that of my own surgical career, has been in the field of anaesthesia. Anaesthesia has been advancing since its introduction in 1846, but the changes that have taken place in this field in the last twenty years exceed those of the previous ninety. In my first ten years as an assistant surgeon many of my difficulties during the operation, much of my post-operative morbidity, and perhaps a quarter of my post-operative deaths were due to the anaesthetic. As a junior surgeon I was unable to secure the services of a trained anaesthetist, and had to depend on the services of any recently qualified man whom my house-surgeon was able to bring in. Most of my patients were terrified when they entered the theatre, struggling during induction, deep purple when they reached the table, stertorous and bubbling throughout the operation, unconscious and motionless during the first six hours after they returned to the ward, vomiting for the next twelve, and

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chesty for the next week. So fearful was I of anaesthetics that for twelve years, from 1927 to 1939, I performed all my gastrectomies and much of my major surgery under local analgesia alone.

The modern anaesthetist gains the patient's confidence by a complete pre-operative overhaul, prepares him by a careful assessment and adjustment of his deficiencies, allays his fears by pre-operative medication, renders him unconscious by an intravenous barbiturate, maintains analgesia by one of the anaesthetic gases, ensures oxygenation and immobility of the diaphragm by controlled respiration, and by the use of relaxants provides the degree of muscular relaxation needed at any stage of the operation. He is no longer a mere "dope merchant." He takes over the whole responsibility for the patient's welfare and the surgeon's peace of mind. He presents the operator with tissues in a condition to suit him, relieves him of all anxiety except for the technical details of the operation itself, and hands him back a patient alive and well.

There is no question that Ogilvie's opinion is shared by all the greater and more skilful surgeons of today, nor is there any doubt that the great decrease in mortality and morbidity, following surgery, is in large measure due to better anaesthesia. I do not believe that the surgeon of today is more skilful or dextrous than were those of the late nineteenth or the early twentieth century. In fact, I think they are a great deal less so, as men like Halsted, Lane, and Lister had to work against all sorts of difficulties caused by inadequate anaesthesia. Necessity for speed was paramount and I am told that even in this country it was quite common to amputate a leg in from three to five minutes. Many of the operations which have been reintroduced today were attempted and occasionally performed successfully fifty years ago, but could not be carried out satisfactorily with the anaesthesia practised at that time.

Certainly we have come a long way along the road. What of the future?

When you ask me what are the essential qualities of an anaesthetist, I presume that you mean a perfect anaesthetist, and one realizes full well that such a paragon does not exist; but at least we should strive to produce him. I think that you will agree with me that in the future anaesthetists and surgeons will share equal responsibility and receive equal compensation for a patient's welfare and if you wish as perfect a surgeon as possible to operate on you, it would seem only fair to expect the same of the anaesthetist.

Sympathy, honesty, strength, and skill—in that order—are the primary requisites of any able man, regardless of his calling, but these qualities are, perhaps, particularly desirous in an anaesthetist. Let me elucidate a little. A patient is naturally terrified at the thought of an operation, but perhaps most frightened of the thought that he must go to sleep, not of his own free will, but on the initiation of someone else, and the horrid spectre is immediately conjured up that he may never wake again, or even if he does, that something dreadful may have happened to him in the meanwhile without his being able to protest. Therefore, I would place sympathy, and I mean it in the true sense of the word—kindness and understanding—as the first quality to be desired. To be able to allay a person's fears, one must first be able to understand the individual and to put one's self in the patient's place. Once this is done, it is relatively easy to discount, one by one, the various "bogeys" which arise, and to all intents and purposes one has control of the patient's mind. I am sure you know enough of the

tricks of the hypnotist to realize that they are little more than this power carried to an extreme degree.

Honesty I think is an essential. It is useless to tell a patient that really he is just going to have a little anaesthetic or a little operation. To him it is a terrifying experience and it is far better to place the cards on the table, to explain exactly what is likely to happen, and what methods you propose to use for combating any dangers which may arise. It would seem wise to explain that he may awake to find himself with tubes protruding from every orifice in his body, and possibly with four or five needles introduced at various points through which solutions are running into him. There may be a mask or two over his face and a tent to cover all. If the patient has a clear understanding that this is all in the nature of things, and to be expected, he will usually accept it with calmness, feeling that the things which have been predicted have come true.

The late Dr. Elder once said that prognosis was infinitely more important than diagnosis. If you tell a patient, or his family, that he is going to die, you should make sure that even this comes true! While I would not recommend that you achieve this drastic result too often, I do feel that honesty certainly pays in your profession, as it does in ours.

Strength is a curious word and one often ill understood. We are not discussing the physical strength of the bull or the bully, or the economic strength of the stock market manipulator but the great moral strength which allows an individual to give confidence and peace to those who are ill or in trouble. This moral strength is indeed a phenomenon, difficult to define, yet of which we are extremely conscious. All who listened to Churchill deliver his famous speech before the fall of France could not help but be almost physically aware of the essential strength of the man and his belief, and themselves felt more capable of carrying on because of some almost metaphysical stimulus which he had imparted to them. This has been true of many of the great prophets and leaders throughout all time, and while one does not expect every anaesthetist to be able to rise to the heights on every occasion, nevertheless I feel that I, myself, would be terrified if I were about to be put to sleep by a timorous man!

Strength may exist in some fortunate individuals from birth, but it can be amplified by knowledge and by the feeling that one is doing the best possible thing that can be done for the patient.

The most controversial essential is skill. No doubt you raise your eyebrows because I name this fourth and not first. So much emphasis has been laid on skill, and I should be the first to agree that without some measure of skill, all the sympathy, honesty, and strength would be useless, but I feel that stress laid on its importance has tended to dwarf the other three essentials. Medicine is not only a science, it is an art as well. However, we must accept the ability to perform one's job, an ability acquired through hard work and orthodox training, as certainly an essential in any trade or profession.

There are many different kinds of skills and it is almost impossible in a single lifetime to learn, or remember, them all. Dr. Penfield once stated that the brain was an organ for forgetting rather than for remembering—and although all of you, I am sure, did extremely well in your various primary courses during your

college days, I wonder how many of you could rapidly enumerate the forty-two centres of the sense of smell, the comparative anatomy of dogfish and frog, the declension of a Latin noun, or even solve a simple problem in algebra. To try to help one's children with their homework is often a humiliating if stimulating task!

Although, therefore, it is desirable to have a good general knowledge of all subjects relating to medicine, because certainly this makes life more interesting, it is essential that you, like us, should concentrate to a certain extent at any rate on special subjects affecting your own specialty. Thus, I think, you will agree that some knowledge of physiology is almost essential to a good anaesthetist, particularly the physiology of respiration and circulation, whereas such knowledge is not so important to, let us say, the orthopaedic surgeon. It would seem important, too, that you have some general idea of physics, as you are dealing to such a large extent with gases and other inorganic compounds.

Must you know all about every disease which the body can contract and be competent to make a diagnosis by history and physical examination in each patient you are asked to see? Many think you should. Some physicians and surgeons, on the other hand, are often apt to take umbrage when an anaesthetist decides to make a complete preoperative examination of their patient. They feel it is none of his business and perhaps are secretly perturbed that he might turn up something they have missed!

Your best course of action probably lies between not seeing the patient at all and taking him over completely.

Skilful diagnosticians and therapists, very often, make a correct diagnosis and suggest treatment from facts related to them over the telephone and there seems no reason why, if you have confidence in a physician or a surgeon, you should not accept his findings and relate them to the type of anaesthetic that you desire to use, looking only for the extra information you may require. It would seem only necessary to amass a separate detailed history and physical report if the patient appears, from the record, to be very ill. In such a case the anaesthetist might wish to have certain special examinations made with a view to determining the risk involved. This, perhaps, can best be done in consultation with the physician, or the surgeon, concerned.

As regards the actual technique of giving anaesthetics, I have little to say. Very like surgical operative techniques, anaesthetic technique is perhaps the least important part of the whole job. Nevertheless, you become very bored and sometimes quite irritated by a surgeon, who cannot or will not get on with his job simply because he is too lazy or lacks the necessary skill; so too it would seem that there is still room for improvement in the technique of some anaesthetists with whom I have come in contact, particularly in their ability to introduce needles into veins quickly, or to enter a spinal canal without having the patient jump off the table and fracture his skull.

Another technique which, I have noticed, is not always perfect, is the insertion of an intratracheal tube, and I have had to explain to patients on several occasions (I must say not without some chagrin) why two or three of the best

front teeth in the world are missing, this being necessary to the success of the operation!

It would seem, too, that considerable care should be taken before the operation begins to place the patient in a position where veins are accessible, even though the surgeon ridicules the idea. He will be the first to blame you if an arm has to be produced from under the drapes thereby forcing him to stop his headlong course. During the operation it would seem unwise to suggest to this poor benighted creature, just after he has divided the common duct, ligated the aorta by mistake, or committed some other such fearsome error, that the patient is not doing very well! Nothing is more apt to spread alarm and despondency throughout the whole team. Do what you can to help and when the emergency is over, tactfully suggest that mayhap today is not the one slated in the stars for the completion of this particular operation.

As far as the postoperative care is concerned we have in this hospital, as you know, a Recovery or Resuscitation Room, whichever you prefer, which has perhaps made the greatest single contribution in decreasing our mortality and morbidity since the war. There was a good deal of criticism by many of the surgeons when we decided to place this room in charge of the Chief Anaesthetist. However, a happy compromise was reached when it was agreed that the surgeon should have the right, at any time, to go in and write the orders for his patient. The anaesthetist would only issue the necessary instructions if the surgeon failed to do so. Needless to say, since the Recovery Room has been opened, to my knowledge no single order has ever been written by a surgeon, and the Recovery Room is now universally approved by everyone. Surely this is a great tribute to the progress of anaesthesia.

What other skills should an anaesthetist have?

Presumably the ability to diagnose peripheral vascular diseases and assess the value of his blocks on such conditions. He must, too, have a wide knowledge of anatomy in order to use local anaesthetics properly.

He must necessarily be a well-trained and imaginative research worker because, after all, anaesthesia is but at the beginning of its road. There is no reason, it would seem to me, why since you gentlemen have mastered the problem of artificial sleep, you should not solve the riddle of natural sleep and relaxation, and thereby save all of us from having the diseases which tension is so likely to cause at the present time.

The following group of qualities do not, perhaps, fall into the realm of actual skills but surely a good anaesthetist should be master of them all. He should have infinite patience, even though suffering the most frightful boredom when a long-winded, laborious, slow-witted surgeon takes hours to do things which he, himself, could do in minutes! He should have a sense of humour capable of gently pacifying the most ruffled nurse and yet he must be careful not to use this at a time when a laugh is like the rasping of a file on the jangled nerves of a surgeon faced with a situation from which he has no idea how to extricate himself. The good anaesthetist must have the ability to get along with his fellow men and women, and be capable of organizing his department so that everyone is com-

pletely happy, and yet accomplish this in such a way that he makes everyone else feel they are actually handling the situation. In other words, he must learn to be a co-ordinator, not a director. He must be adaptable, a quality well illustrated by what occurred during the past war, when one was transported from all the comforts and assistances which were provided in civilian life into makeshift operating rooms and quarters where one literally had to scrub the floors before one could even start to think of one's own equipment.

Undoubtedly, the essential qualities of an anaesthetist must vary depending upon the situation in which he finds himself. Whereas in a university hospital he should have all the qualities previously described plus the ability to teach, in a smaller hospital some of these are not essential and others only to a moderate degree.

Just recently I asked the wife of a friend of mine whom I had trained and who is now doing surgery in a large town, how he was getting on. To my astonishment she burst into tears and said she was terribly disturbed because he had lost three of his last twelve gastrectomies and she wondered if he should not return for further training. I asked her a few questions about the hospital and the community and my suggestion to her was a simple one, that my friend should take some of the money which he was rapidly accumulating and associate himself with a first-class anaesthetist. I felt then that his troubles would be over. In fact he accepted my suggestion, the desired result has been achieved, and his income has increased greatly despite the added expense.

I know perfectly well that you realize that what I have said is partially in a joking mood because it must be obvious to you, as it is to me, that a man possessing all the qualities which I have enumerated would not be a man at all but a veritable god. However, I have at least attempted to outline the possibilities that you may all strive for. As Browning said,

> Ah! but a man's reach should exceed his grasp,
> Or what's a heaven for.

In summary one might say:

Show me a man with sympathy, honesty, strength and a moderate amount of skill, who is interested (1) in the welfare of the patient, (2) in the team of which he is a part, and (3) in the profession of medicine as a whole and in the institution to which he belongs, and I am quite certain not only that he will have the essential qualities of a wonderful anaesthetist but that his own success and that of the anaesthesiology in his community will be assured.

Résumé

Les qualités qui définissent un homme de valeur quelque soit sa profession et qui sont particulièrement essentielles chez l'anesthésiste sont la sympathie, l'honnêteté, la force et l'habilité.

La sympathie dans le vrai sens de l'amabilité et de la compréhension est essentielle si l'on veut apaiser la crainte naturelle du patient pour un sommeil que ne vient pas de lui mais par la volonté d'un autre.

L'honnêteté s'impose. Il est inutile d'essayer de faire croire au patient qu'il va avoir seulement une courte anesthésie ou une petite opération quand pour

lui n'importe laquelle opération est terrifiante. Il est préférable de lui dire exactement ce qui va se passer.

La force morale requise est celle qui inspire confiance et paix à ceux qui sont malades ou qui ont du troubles. Elle se définit difficilement bien qu'on la détecte aisément. De tous les temps, cette qualité a été un attribut des grandes chefs. On ne doit certes pas s'attendre que l'anesthésiste atteigne le sublime à chaque occasion; il n'en reste pas moins qu'on serait effrayé à la pensée d'être endormi par un homme timoré.

L'habilité est la qualité qui soulève le plus de controverse. Bien qu'il soit vrai que sans l'habilité, la sympathie, l'honnêteté et la force morale seraient inutiles, il n'en demeure pas moins vrai que l'habilité est la qualité la plus facile à acquérir. D'autre part la force s'augmente quand on a la connaissance et l'habilité qui donnent le sentiment qu'on fait le mieux possible pour le patient.

En plus de ces qualités majeures, l'anesthésiste doit posséder de la patience, le sens de l'humour et doit être capable de s'accorder avec les autres gens.

Qu'on me montre un homme qui est sympathique, honnête; qui a de la force morale et qui est suffisamment habile; qui s'intéresse au bien-être du patient, à l'équipe dont il fait partie, à la profession médicale elle-même et enfin, à l'institution pour laquelle il travaille — cet homme j'en suis certain, a les qualités essentielles pour être un merveilleux anesthésiste.

A NEW APPROACH TO THE CONTROL OF SHOCK

ELIZABETH M. MARTIN, M.D.*

THE solution to the problem of shock may have been within our grasp ever since sympathetic blockade first occurred as a corollary to spinal analgesia. Labat's monograph in 1931 cites the use of spinal analgesia without a pressor drug to combat shock resulting from crushing injury (1). Since the circulatory system is dependent chiefly on gravity in high subarachnoid block, anaemia of the brain is prevented by the Trendelenburg position. In this position it is both neurologically and anatomically impossible for the solution to diffuse to the respiratory centres (1).

We can produce autonomic block with "total spinal," with Hexamethonium compounds and Arfonad®, or with Chlorpromazine. The latter are easy to use, readily transportable and can be administered without further moving of the patient. We have done a large volume of clinical work with "total spinal" induced hypotension, using the technique introduced by Griffiths and Gillies (2; 3). The spinal induced hypotension is capable of blocking the sympathetics, establishing analgesia, giving muscle relaxation and control of haemorrhage by positioning, all in a single manoeuvre. The Hexamethonium technique calls for a relaxant and an anaesthetic drug if reparative surgery is contemplated (25; 26; 27). Chlorpromazine acts as an autonomic blockade, a hypothalamic depressant, and is an excellent pre-medication agent (4; 5; 6; 7).

Immediately following injury the alarm goes out to the circulatory system to preserve the blood volume. Anatomically one thinks of the vascular tree as a single system. Physiologically it immediately becomes two systems (10): a "peripheral" pool which can be spared, and a "central" pool, which must be preserved. After injury, a preferential blood shift takes place, and the peripheral blood pressure drops, as measured over the brachial artery by cuff and manometer. When a total sympathetic block is induced in man the peripheral blood pressure also drops, but for a wholly different reason. That is why one speaks of induced hypotension rather than ganglionic block, although this is only the most spectacular effect. This drop in peripheral pressure is just as capable of killing the patient as trauma or actual blood loss because the body no longer has the ability to decide where the blood is most needed. We must make the decision and can then maintain an adequate blood supply to the vital organs by a complete head-down tilt of the body in a 15-degree Trendelenburg position. If this is not possible, raising the legs above the level of the trunk with the head flat will suffice. In the unconscious intact human, with a ganglionic block to the first thoracic nerve root, placed in a 15-degree Trendelenburg position, the systolic pressure is read by oscillation between 90 and 120 mm. Hg. This appears to be irrespective of previous hypertension or hypotension, as we have observed in 680 cases given spinal analgesia without a pressor drug to the level of the first

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thoracic nerve root. This blood pressure measurement represents the total pressure under block of an apparently normal blood volume. Therefore, in replacing blood for the shocked patient, when the total blocked pressure, which may have been unobtainable, returns to the level of 100 mm. Hg. systolic, the blood volume has been adequately restored.

If a patient has a penetrating abdominal wound with internal bleeding, or one leg nearly torn off with the iliac artery pumping blood up behind the peritoneum, or if a woman has an obstetrical haemorrhage, the wound is central and the bleeding is increased by the peripheral vasoconstriction of the protective mechanism. If such a patient is given 100 mg. of Hexamethonium Iodide intravenously, a fairly complete ganglionic block follows in 2–5 minutes. During this time, the bleeding area is elevated to the highest point if possible, while the patient is placed in Trendelenburg position until the pressure can be determined. If it is above 70 mm. Hg., then, while blood is given, it will be safe to reposition the patient in such a way that the operative site takes advantage of the ischemic effect of a posture in the patient with a block. If the total blocked pressure in Trendelenburg position is less than 50 mm. Hg., then the arms may also be elevated to take advantage of the blood which has pooled there. Intravenous replacement is made as rapidly as possible until the pressure is read between 50 and 60 mm. Hg. Establish anaesthesia with the agent of choice or availability, giving oxygen wherever possible. We have used Cyclopropane, Nitrous Oxide-Oxygen, and even Thiopentone in very dilute solutions (gm. 1 in 1000 cc. normal saline) given cautiously when gas was not available. Ether is contraindicated as it interferes with capillary vasomotion (12).

The surgeon takes advantage of the bloodless field to repair damage while vasodilatation averts anoxia of the vital organs. This technique will delay the onset of irreversible shock and will minimize the sequelae of anoxic tissue damage which are too often the price imposed by nature for survival (21). In the patient whose mechanism has compensated for his shock, a second insult, such as surgery, without the protection afforded by a vasodilated system may throw him into the phase of irreversibility, as in the second bleeding of the experimental animal.

This concept of the treatment and control of shock is supported by evidence of two kinds: that of experimental physiologists who have seen these phenomena for some time without attempting the clinical application, and that of the clinicians who have stumbled upon it, and been too frightened by its complete reversal of all we have previously been taught to put it into operation. Foldes (13) has pointed out that it is almost impossible to bleed a dog with ganglionic block into the state of shock provided the bleeding point does not lie below the level of the heart. It does not matter whether the block is with a spinal agent or a Methonium salt. The most striking manifestations of haemorrhagic shock will actually be inhibited by a total sympathectomy because the usual preferential blood shift to the vital organs no longer occurs (14; 28). Selye further states that, in the dog, Dibenamine decreased the incidence of irreversible shock after extensive haemorrhage or trauma (15). In experiments where various protective measures, such as Dibenamine or sympathectomy, have been introduced the venous outflow from the omentum into the portal system is remarkably well

sustained, even at blood pressures as low as 30 mm. Hg. The essential difference between Dibenamine-treated and etherized dogs subjected to shock is the continued operation of the terminal vascular bed as a dynamic functional unit in the Dibenamine-treated animal which is resistant, and the functional deterioration of the peripheral circulation in the etherized animal which readily develops the irreversible type of shock (12). Dibenamine is no longer protective if given after shock has developed. This confines a promising drug to the laboratory. We do have, in its place, Chlorpromazine, which combines an effective adrenergic blockade with an autonomic blockade and a central depressant effect at the level of the hypothalamus. Experimental and clinical work carried out by Laborit and his co-workers in France proved it very effective in the control of shock by a mechanism similar to that of Dibenamine, sympathectomy, total spinal, and Methonium compounds (16; 17; 18; 19). From a neurosurgeon's experience with the central nervous system and shock, as reported by Franklin (20), comes an interesting observation which may shed additional light on the role of Chlorpromazine. Shock was not produced with the removal of, or trauma to the cerebrum as far down as the thalamus, or with increased intracranial pressure. Shock occurred only during operative interference in the region of the optic chiasma with attendant retraction of hypothalamic structures. Manipulation of the brain stem even at the supposed level of the vasomotor centre produced no effect upon blood pressure.

In the early stages of the shock phase, adrenergic peripheral vasoconstriction will expedite the onset of irreversible shock due to the elaboration of Ferritin (V.D.M.). Following even arterial transfusion, the arterioles become atonic and distended, the capillary circulation remains slow despite blood pressures as high as 100 mg. Hg. systollic, and progressive pooling of blood on the venous side of the bed develops. If the transfusion is continued, pulmonary oedema and cardiac dilatation occur without resuscitating the animal (12; 20). This was also seen in battle casualties.

If one can put all of the shocked patient's available blood volume at the service of the vital organs, in such a manner that he can make full use of its oxygen carrying power through a non-resistant vascular bed, whose capillary vasomotion remains undisturbed (29), that patient can make better use of half his original blood volume with the vasodilatation provided by ganglionic blockade than he could with his reduced blood volume in the presence of vasoconstriction (21). Animals treated with Dibenamine can be recovered by replacement of as little as 50 per cent of the total blood withdrawn during haemorrhage (12; 20). By proper positioning we must see that we do not allow the patient to bleed into his own vascular reservoir.

Pitkin has reported two urgent emergencies: the first, a ruptured spleen and the second, a cut bowel with a severed internal iliac artery from a knife wound. Both of these were given high spinal anaesthetics, which he considered life-saving, as they permitted quick control of bleeding, response to intravenous infusions, and immediate surgery (11).

When Hexamethonium Chloride is used clinically, Rollason (22) says, "In the acute head-up position with a 30–40 degree tilt in reverse Trendelenburg position,

the systolic blood pressure should not be allowed to fall below 79–80 mm. Hg. to avoid an oxygen debt to the brain." In a 15-degree head-up position an average reduction of 44 per cent in mean arterial blood pressure failed to alter cerebral blood flow or oxygen consumption, which was maintained by a 46 per cent reduction in cerebrovascular resistance (29). (The head-up position may *never* be used in a high spinal block.) Always test the person before elevating the head. Therefore, if the wound be of the head and neck, the head and neck should be elevated and the blocked pressure determined in this position. If it is below 70 mm. Hg., replacement with blood, plasma, or plasma substitutes should be rapidly accomplished until the pressure can be maintained at this level while the surgeon goes ahead in a comparatively bloodless field.

Because the blood vessels are dilated, they lie open on the cut surface and become thrombosed. When the block wears off, they constrict onto the clot, thereby reducing the likelihood of fresh haemorrhage when the pressure rises. Haemostasis must nevertheless be meticulous before wound closure.

There is evidence to show that Hexamethonium actually protects against shock, as shock has not supervened when it has been used with Cyclopropane and Flaxedil® for long and traumatic manoeuvres with fractured legs in placing Steinman pins or bone plating refractory fragments. This is in comparison to previous experience in using Cyclopropane alone for orthopaedic cases. Shock invariably occurred in these cases unless they were carried at the verge of respiratory arrest for the entire operation. This was before the days of relaxants.

There has been some argument about whether cardiac anoxia might occur with the induced hypotension technique. Rollason (23), citing Wigman, reports a few cases with an "inversion of the T wave lasting for several days before reverting back to normal." N. du Bochet and J. LeBrigand report on a series of electrocardiograms done on decompensated cardiacs under spinal anaesthesia. The patients were all undergoing major abdominal surgery, 15 for ligation of the inferior vena cava. All showed slowing of the pulse rate once spinal block took effect. All Q.R.S. complexes increased from .02 to .04 second under spinal and 12 negative T waves became positive. Studies are in progress to correlate pulmonary artery pressure, minute volume, and arterial oxygen with striking clinical improvement of pulmonary oedema, tachycardia, urinary output, cyanosis, and dyspnoea under spinal anaesthesia. Pulmonary artery pressure was seen to drop 25–42 mm. in two cases, the minute volume to increase up to 1½ litres (24).

After September, 1952, I deliberately applied the ganglionic block technique to control shock in patients felt to be in extremis. Some representative case histories follow:

The first of these histories concerns a case of obstetrical haemorrhage from a retained placenta. The brachial blood pressure was unobtainable, yet blood was still running in a steady stream from the patient's vagina. A transfusion using a vein at the wrist and a No. 18 needle was barely dripping because of the extreme vasospasm, in spite of pressure in the flask. Hexathide® 100 mg. were injected in the intravenous needle *in situ*. The patient was in lithotomy position, which was changed to Trendelenburg-lithotomy position. Anaesthesia was begun with Cyclopropane. Two minutes after Hexathide®, the blood was running freely into her

vein with the release of vasospasm. The blood pressure could be read at 40/10 with a pulse rate of 100. A second 500 cc. of blood brought the patient's pressure in Trendelenburg position to 90/30. We felt that she was out of danger as there was no further bleeding. Her recovery was uneventful. The problem here was not the total blood loss but the fact that the patient was losing blood faster than it could be replaced. Blood replacement should be available as soon as possible, but if it is not yet available, rapid saline infusion or blood substitute will serve as a temporary stop-gap. If the Hexamethonium can be introduced into a small vein with a hypodermic needle, the resulting vasodilatation will enable one to place a needle in a large vein by letting the arm or leg drop over the edge of the table. This saves the time lost performing a cut-down. At the same time, the dangers of arterial transfusion are avoided.

The second case was that of a boy who had suffered a head injury but was just beginning to regain consciousness. The surgeon desired to plate a compound comminuted fracture of the tibia and fibula which appeared to be keeping him in shock in spite of blood replacement. Further brain anoxia was to be avoided. He was given a spinal block with Nupercaine® 10 mg. and Procaine 100 mg. in 4 cc. of spinal fluid, between the second and third lumbar nerve roots. He was immediately tilted into Trendelenburg position. After five minutes, his pressure was 100/30, although it had been 70/40 before the block was induced. He had been trapping some of his available blood supply in his extremities with vasoconstriction from tissue injury. The leg to be plated was elevated on a pillow with a marked reduction in bleeding at the site of fracture; no increase in bleeding was noted from the Cyclopropane with which he was kept asleep. The Cyclopropane was used to assure sleep, thus preventing vomiting as a reflex protective mechanism when a high subarachnoid block is in effect. When he awoke, he appeared much clearer mentally than before, and he made an uneventful recovery.

The third case was an almost exsanguinated ectopic gestation. As the patient was being prepared for the operating room, intravenous saline was begun while blood was being typed and cross-matched. She was barely put to sleep with Pentothal 200 mg. in the intravenous tubing, Cyclopropane anaesthesia was induced, while 100 mg. of Hexathide® and 20 mg. Flaxedil® were given. By the time the surgeons had scrubbed, the Flaxedil® was effective, anaesthesia was established, and a slight Trendelenburg position had been effected. Her blood pressure was still unobtainable, but the intravenous saline had begun to run rapidly and the blood was on its way. Liquid blood, 1500 cc., was suctioned out of her abdomen (measured) besides clots and soaked abdominal sponges. The Fallopian tube was no longer bleeding. By this time, a pressure of about 30/? mm. Hg. was obtainable and the blood arrived. Under pressure we replaced 1500 cc. of blood loss in three-quarters of an hour, and her blood pressure in Trendelenburg position was 100/40, with complete recovery.

The next extremely dramatic case was that of a patient with a ruptured ectopic gestation, arriving at the hospital unconscious, with no measurable blood pressure and an impalpable radial pulse. Fortunately, the gynaecologist had seen her some days previously and was aware of the possibility of an ectopic gestation. She was undressed on the stretcher in the operating room to save time. It was

impossible to locate a vein. She was placed on the right side and Nupercaine® 10 mg. (1:200 in 2 cc. solution) added to Procaine 100 mg. made up to 4 cc. with spinal fluid was given between the 3rd and 4th lumbar nerve roots in a 10-degree Trendelenburg position. She was placed supine on the table and tilted further to 15 degrees. Oxygen with Cyclopropane was started, again to assure sleep where more depressant narcotics were to be avoided. Her respirations which had been gasping and irregular became normal and regular, her colour improved, and when the left arm was dropped over the side of the table, a large vein became readily visible. Subtosan® 500 cc. was started with a No. 18 needle. When 500 cc. of Group O, RH negative blood arrived it was started in the right arm. Her blood pressure at this time was 40/20 mm. Hg. A further 1000 cc. of blood (typed and cross-matched with donors as well as patient) resulted in a blood pressure of 95/40 mm. Hg. A further 1000 cc. of saline was given on the ward. The amount of blood loss could not be determined as a good deal of it went on the floor when the abdomen was opened. We considered that, in this case, spinal anaesthesia had been truly life-saving. Her blood volume had been adequately restored, and the following morning one would never have known she had been in extremis.

In another case of a ruptured uterus where adequate blood replacement had been made for the patient's constricted vascular system to be in compensation at a blood pressure of 130/70, the method of "total" spinal without a pressor drug was chosen in order to minimize further blood loss and prevent the irreversible phase which is seen to supervene after a "second bleeding" of the experimental animal. This was the type of case so often reported from the battlefront with disastrous results even where massive blood transfusions were available. Again the patient recovered without further incident.

We then became bolder and used Hexamethonium Iodide for incomplete abortions if the patients showed signs of shock or were still bleeding. We used it for patients with fractures who had traumatic shock if they did not show adequate response to blood transfusion. Several times when the surgery promised to be minor, but turned out to be major, we saved the patient's blood and prevented shock with "Hexathide®" added to the established anaesthetic. One of these occasions was with a case of abdominal pregnancy, where, after the block became effective, I noticed that the placenta rubbed off the bowel like wet blotting paper, without damaging the serosa. Several patients with extensive abdominal carcinoma were kept alive through perilous operations that allowed them some further months of fairly comfortable life. Radical breast resections were done with an estimated loss of less than 100 cc. of blood.

The next case is an example of one where blood could not be given. We were consulted after the patient, still shocked, and bleeding from the uterus, had developed hives from the first 50 cc. of plasma, and chills and fever following the first 100 cc. of blood. We had some plasma substitute kindly given us by Poulenc Ltd. for such a contingency. To this Subtosan® was added 130 mg. of Pentothal®, 100 mg. of Hexathide®, and anaesthesia was established with Cyclopropane. She was in lithotomy-Trendelenburg position and in spite of this, her pressure was about 30/10 mm. Hg. She stopped bleeding immediately and did

not lose much more with the curettage, but the surgeon asked for Ergotrate®. We had not been using it with these cases because the patients did not appear to need it. With one ampoule, her blood pressure rose to 70/40, whereupon she began to bleed again, and had to be packed. The blood pressure then dropped off just as rapidly, and by the time we had given two bottles of plasma substitute, her pressure was 60/30 in Trendelenburg position. She was given oxygen by tent and continuous saline infusion. After 5 hours, her blood pressure again dropped below 50 mm. Hg. although her pupils were dilated and she appeared still to have some block present. Since she was no longer bleeding we decided to try decreasing the size of her vascular tree. We gave Methedrine 5 mg. at five-minute intervals until 20 mg. had been given, and her blood pressure was 80/40. We put another 10 mg. of Methedrine® into the intravenous drip and her blood pressure stayed constant at about 100 mm. Hg. for the next several days. She had a very stormy course owing largely to a transfusion reaction, having both hives and herpes. She did not sleep with her sedative, and became irrational. In 48 hours she appeared to be normal except for weakness from anaemia. Her haemoglobin was then 40 per cent. She tolerated liver and intravenous iron and progressed well, showing no mental damage from her prolonged hypotension.

We have, during the past year, been investigating Chlorpromazine as an adjuvant to anaesthesia, and in its relation to the control of shock, comparing it with the two methods previously described. Actually it may be used alone or in combination with hypotensive spinal anaesthesia techniques or Hexamethonium. Again, this is an agent whose use results in a vasodilated system. The principles governing its use remain the same as those for high spinal block or Hexamethonium salts.

The following case history is illustrative. A gentleman of some 50 years who had been hit by a car, with a resulting compound comminuted fracture of his right tibia and fibula, right femur and humerus, a fracture of his pelvis and a head injury, in spite of morphine and blood, was in severe shock when seen. He had been given two units of blood and Levophed® without any improvement. He was given 50 mg. of Chlorpromazine intravenously and another 50 mg. intramuscularly. The tibia was plated and the fractures of the femur and right humerus were set temporarily under Cyclopropane anaesthesia. At the end of the operation he was warm and dry with a blood pressure of 100/70. He complained very little of pain. A minimal amount of Demerol® kept him comfortable. This patient had two subsequent anaesthetics, one for Kunchner nail to the femur and another for setting the humerus. He showed no gross mental changes in spite of his head injury. Chlorpromazine was chosen here to offset the effect of Levophed® and establish sympathetic block.

It would have been of immense scientific interest to have been able to determine the presence or absence of V.D.M. in the blood streams of these shocked persons. Clinically, there is no doubt in our minds that a hypotensive technique provides a wider margin of safety for the injured, and may completely prevent the occurrence of the irreversible phase of shock.

Over the past two years, we have lost only two patients for whom we have been called when the surgeons felt the situation was out of control. Both of these

patients were children with post-tonsillectomy haemorrhage, who were seen so early in our work that we lacked the courage of our convictions and attempted resuscitation by arterial transfusion. In the first case this resulted in pulmonary œdema and cardiac dilatation and death for the child without any improvement having occurred in his circulatory status. The second child died of a transfusion reaction although the blood given was correctly matched as far as our laboratory could determine even on rechecking. Our later experience taught us that while the survival of the first child might have been problematical, the second child's circulatory system could have been stabilized and his bleeding stopped by the use of Hexamethonium.

I should like to add one more striking case history: that of a female, age 52, thought to have been hit by a car. There was an obvious fracture of the left femur and left humerus. She was said to have Hodgkin's Disease as well. When seen she was deeply shocked, and lapsed into coma just after being seen. Demerol® 100 mg. and Chlorpromazine 50 mg. were given intravenously, one after the other. The X-ray table was placed in 10-degree Trendelenburg and oxygen was given by mask from the gas machine. The patient stopped breathing spontaneously for 10 minutes. At the end of that time a facial pulse was again felt and she began to breathe spontaneously. The X-ray revealed pathological fractures of multiple myeloma. It subsequently developed that she had fractured each one of her long bones. With Nitrous Oxide–Oxygen anaesthesia the patient was put in traction in Trendelenburg position and supportive fluids only were given—no blood. She maintained a pressure of 70/40 which gradually rose to 100/80 in the next 24 hours. She was kept on Chlorpromazine 25 mg. every 4 hours, with Demerol® as needed. On the second hospital day she was given blood because of the severe anaemia and low Hematocrit. She had at no time any kidney block and no mental deterioration. This patient is still alive. While I must apologize for being available to save such a patient, perhaps it was permitted in order to convince us that the impossible is possible.

Discussion

It has been pointed out that the blood pressure seen in sympathetic blockade for hypotensive anaesthesia may frequently be anywhere from 50 to 30 mm. Hg. systolic over the brachial artery. This low pressure is obtained by pooling some of the patient's blood into the lower extremities while the head and trunk are kept in a down-tilt. In fact the anaesthetist has artificially produced a situation in which 1000 to 1500 cc. of the patient's available blood volume are lost to him in terms of actual use by the vital organs. This loss does not cause the anaesthetist any alarm, nor does it harm the patient. If with a spinal block there is a decrease in pulse rate below 60 per minute, or if with the drug-induced blockade there is a further blood pressure drop below the established level, then more blood is required and may be instantly given by elevating the feet. Therefore when the patient who has lost, from traumatic injury, some undetermined portion of his blood volume is given a sympathetic block and placed in Trendelenburg position, the resulting blood pressure reading will immediately indicate how severe that

loss has been, and how urgent is the need for blood replacement. At the same time it makes the technical problem of replacing it much easier.

This is a method whereby we can regain control of the shocked patient's circulatory system when shock has progressed beyond our control and appears to be approaching the irreversible phase. In these patients where one must trust clinical judgment we hold that there is now a further chance for life. If this method should prove itself safe in other hands than mine for the patient who is lost without it, then increasing experience may widen the scope to a point where it may be used as first choice in severe trauma rather than a last resort.

Summary

A method for the control and alleviation of traumatic and haemorrhagic shock is presented, using the principle of vasodilatation by sympathetic blockade obtained variously by high subarachnoid block, Hexamethonium compounds, or Chlorpromazine. By using position and blood replacement therapy in conjunction with sympathetic blockade it is possible to arrest and reverse the shock phenomena more promptly and safely for the patient and render immediate surgical interference feasible for repair of injury.

Résumé

Il a été démontré que le choc résultant d'un traumatisme et de l'hemorragie peut être controllé par un blocage sympathique produit par une infiltration subarachnoide spinale haute, ou encore, par les composés de l'hexaméthonium, l'arfonad et le chlorpromazine pourvu que l'on place le patient de façon à utiliser la vasodilatation résultante.

Le traumatisme est suivi d'un déplacement sanguin qui se traduit par une chute de la pression périphérique comme on peut le constater au sphygmomanomètre au niveau de l'artère brachiale. Ceci est dû à la vasoconstriction périphérique. De même, quand on produit un bloc total du sympathique chez l'homme, la pression artérielle périphérique tombe aussi mais cette fois pour une raison complètement différente. . Il est possible, en cette circonstance, de maintenir un apport sanguin adéquat aux organes vitaux, en plaçant le patient en Trendelenburg à 15° ou bien en élevant les membres inférieurs au dessus du viveau du thorax, la tête étant maintenue à plat. De cette façon, la circulation se maintien à une pression diminuée et la réduction de la résistance vasculaire compense et permet de préserver une oxygénation adéquate.

Dans les cas d'une blessure centrale où l'hemorragie est augmentée par la vasoconstriction périphérique produite par les mécanismes de défense, une injection intraveineuse de 100 mgm d'iodure d'hexaméthonium réalise un blocage ganglionaire presque total en 2 à 5 minutes. La vasodilatation résultante permet de trouver une veine, de commencer une transfusion de remplacement et aussi d'élever la région qui saigne en maintenant la tête et le thorax abaissés. Une anesthésie peut être donnée avec n'importe lequel agent excepté l'éther qui perturbe la vaso motricité capillaire.

Chez le patient dont le mécanisme protecteur a compensé pour le choc, une intervention chirurgicale qui se priverait de la protection procurée par une vasodilatation systémique, peut le conduire dans une phase de choc irréversible.

Quand on utilise les composés de l'Hexaméthonium ou le Chlorpromazine, on peut maintenir la position tête élevée, à condition que la pression brachiale artérielle ne descende pas en bas de 70 mm de Hg. S'il y a chûte, une restoration rapide au viveau désiré s'obtient par le plasma ou ses substituts.

Depuis septembre 1952, j'ai employé cette méthode pour contrôler le choc de patients que les chirurgiens ne croyaient pas devoir survivre en défit des mésures thérapeutiques qu'ils avaient déjà instituées. Ces cas étaient traumatiques, hemorragiques ou encore, mixtes. Ils furent traités par un blocage rachidien haut, aucune médication vasoconstrictive n'étant employée; ou encore par l'iodure d'Héxaméthonium ou le Chlorpromazine, selon les circonstances. Par cette méthode, il est possible de reprendre contrôle du système circulatoire du patient en état de choc quand ce choc a progressé au delà de notre contrôle et semble approcher la phase irréversible.

REFERENCES

1. Labat, Gaston. Nelson's Loose Leaf Surgery, vol. I. London: Nelson (1931).
2. Griffiths, H. W. C. and Gillies, J. Thoracolumbar Splanchnectomy and Sympathectomy: Anaesthetic Procedure. Anaesthesia 3: 124 (1948).
3. Gillies, J. Hypotension during Anaesthesia. Lancet *1*: 325 (1953).
4. Huguenard, P. Hibernation artificielle: nouvelles données utiles. Anesth. & analg. 9: 240 (1952).
5. Courvoisier, S., Fournel, J., Ducrot, R., Kolsky, M. et Koetschet, P. Propriétés pharmacodynamiques du chlorhydrate de chloro-3-(dimethylamino-3-propyl)-10-phenothiazine (4560 R.P.). Arch. internat. de pharmacodyn. *92*: 305 (1953).
6. Hudon, F. and Jacques, A. Artificial Hibernation. Proc. Canad. Anaesth. Soc. (1953).
7. Huguenard, P. Essais de vasoplégie par l'association de drogues. Anesth. et analg. 9 (1952).
8. Wiggers, C. J. Am. Heart J. *33*: 633.
9. Hale, Donald E. Controlled Hypotension by Arterial Bleeding during Operation and Anesthesia. Anesthesiology 9: 498–505 (1948).
10. Payne, J. P. Controlled Hypotension in Theory and Practice. Brit. J. Anaesth. *25* (April 1953).
11. Pitkin's Conduction Anesthesia. Ed. by Southworth and Hingson. Lippincott (1946).
12. Josiah Macy Jr. Foundation. Symposium on Shock and Circulatory Hemostasis (1951).
13. Foldes, Francis F. The Role of Cholinesterase in Anesthesiology; lecture at Congress of Anesthetists, Virginia Beach, Sept. 1952.
14. Morris, C. G. Jr., Mayer, J. H., Snyder, H. B., Hynes, B. W. Jr. Vascular Dynamics in Controlled Hypertension. Ann. Surg. *138* (Nov. 1953).
15. Selye, Hans. Stress. Montreal: Acta Inc. (1950).
16. Laborit, H. Lecture at Toronto General Hospital, Nov. 1953 and personal communication.
17. —— L'Hibernation artificielle en anesthésiologie. Anesth. et analg. 9 (supp. 1952).
18. Laborit, H. et Huguenard, P. Technique actuelle de l'hibernation artificielle. Presse méd. no. 68: 1455 (1952).
19. Laborit, H., Jaulmes, C. et Benitte, A. Quelques aspects experimentaux de l'hibernation artificielle. Anesth. et analg. 9: 232 (1952).
20. Josiah Macy Jr. Foundation. Symposium on Shock and Circulatory Hemostasis (1952).
21. Gillies, J. Anesthetic Factors in Causation and Prevention of Excessive Bleeding during Surgical Operations (Clover Lecture). Ann. Royal College Surgeons of England 7: 204–21 (1950).

22. ROLLASON, W. NORMAN (Hull, England) quoting Park, paper read at Congress of Anaesthetists, Virginia Beach, Sept. 1952.
23. —— quoting Wigman.
24. DUBOUCHET, N. and LE BRIGAND. Anesth. & Analg. (May-June 1952).
25. COX, R. Hypotension during Anaesthesia. Lancet *1*: 325 (1953).
26. DAVISON, M. H. A. Pentamethonium Iodide in Anaesthesia. Lancet *1*: 252 (1950).
27. ENDERBY, G. E. H. Controlled Circulation with Hypotensive Drugs and Posture to Reduce Bleeding in Surgery: Preliminary Results with Pentamethonium Iodide. Lancet *1*: 1145 (1950).
28. FREEMAN, N. E., SHAFFER, S. A., SCHECTER, A. E. and HOLLING, H. E. The Effect of Total Sympathectomy on the Occurrence of Shock from Hemorrhage. J. Clin. Investigation *17*: 359 (1938).
29. STONE, H. H., MACKRELL, T. N., and WISCHLER, R. L. The Effect on Cerebral Circulation and Metabolism in Man of Acute Reduction in Blood Pressure by means of Intravenous Hexamethonium Bromide and Head-up Tilt. Anesthesiology *16*: 168 (1955).

NISENTIL IN CYSTOSCOPY*

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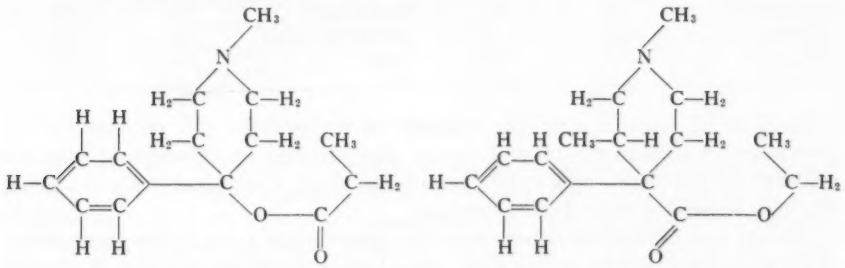
WITH the synthesis of Nisentil in 1947 by Ziering and Lee (1), and the study of its pharmacological properties by Holland and Gross (2), and Randall and Lehmann (3), many different clinical uses have been prescribed for this drug. The new analgesic drug has been advocated for the relief of pain, for analgesia in obstetrics (4, 5, 6, 8), for preanaesthetic medication, and for short surgical procedures including cystoscopy (7). It is the purpose of this study to assess the value of Nisentil as an alagesic agent for cystoscopy and retrograde pyelography.

Before proceeding with our study it would be profitable to review the pharmacological properties of Nisentil. The drug is a synthetic homalogue of Demerol and structurally they are closely related, both having basically a 4-phenyl piperidine structure. This is shown in Figure 1.



Demerol Nisentil

FIGURE 1

Nisentil is an analgesic which is more potent than Demerol but less potent than morphine (the effective dose is between 30 and 60 mg.). Its sedating effect is moderate, and also lies between those of morphine and Demerol. The respiratory centre is depressed by the drug especially in the presence of other opiates or barbiturates. There is little effect on the cardiovascular system with only slight fluctuation of blood pressure and pulse rate. Decrease of the respiratory minute volume is through the depression of the respiratory centre. The effect is mainly on the rate, especially with larger doses. The onset of action is rapid, from 1 to 5 minutes (7) when administered intravenously and 3 to 15 minutes (6) intramuscularly. The duration of action is brief, varying from 1½ to 2 hours.

METHOD

Clinical observations on the analgesic effects of Nisentil were made on patients undergoing cystoscopy and pyelography. The subjects comprised a random selec-

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tion of patients who were admitted and discharged the same day from the hospital, outpatients, and regular hospital inpatients as illustrated in Table I. There were 34 per cent outpatients and 66 per cent inpatients, their ages ranging

TABLE I

NISENTIL FOR CYSTOSCOPY

	Nisentil	Nisentil–Pent.	Nisentil–Pentothal Nitrous Oxide	Total
Cases	76	38	21	135
Per cent	56	27	17	100

	Cases	Per Cent	Premedication with Opiates	Cases	Per Cent
Inpatients	88	66	Premedicated	91	68
Outpatients	47	34	Not premedicated	44	32
Total	135	100	Total	135	100

from 12 to 83 years of age. The majority of the patients (68 per cent) were premedicated with morphine or Demerol plus atropine or hyoscine and the remainder (32 per cent) with only a belladonna drug. Premedications were given one hour before the anaesthetic procedure.

Nisentil was administered intravenously immediately prior to the preparation of the patient for surgery so that there was a lapse of approximately 3 to 5 minutes before the insertion of the cystoscope. The effectiveness of the analgesia was judged by both subjective sensations of the patient and objective findings of discomfort such as movements, grimaces, moaning, etc. Dosage of Nisentil ranged from 30 to 60 mg.; repeated small doses of 10 mg. may be injected when initial analgesia is found to be inadequate.

In our second group, Nisentil was administered intravenously as above in doses of 30 to 40 mg. before the preparation of the patient. Pentothal or Surital was then injected in small hypnotic doses just before the insertion of the cystoscope. Usually no further injection of Pentothal was required after the initial insertion of the cystoscope.

Finally, in the third group, Nisentil was combined with Pentothal and Nitrous Oxide, which was administered throughout the procedure so that the patient was completely anaesthetized for the duration of the examination.

RESULTS

Of the 30 male and 46 female cases (Table II) of cystoscopy and pyelography handled with Nisentil alone, 66 cases, or 87 per cent, were completed satisfactorily without other supplementary agents. Nisentil afforded complete analgesia with no discomfort in 42 per cent of the cases in which there were 30 per cent of

TABLE II

DEGREE OF ANALGESIA WITH NISENTIL

	Satisfactory								Unsatisfactory	
	No Discomfort		Slight Discomfort		Moderate Discomfort		Total		Total	
	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent	Cases	Per Cent
Male	9	30	13	44	5	13	26	87	4	13
Female	24	52	15	32	1	2	40	86	6	14
Total	33	42	28	37	6	8	66	87	10	13

Side reaction	Cases	Per cent
Dizziness	4	
Nausea and vomiting	1	
Cheyne-Stokes respirations	1	
Total	6	8

the male and 52 per cent of the female cases. In 37 per cent of the cases there was slight discomfort; among these were 44 per cent of the males and 32 per cent of the females. In 8 per cent of the cases there was moderate discomfort initially, but this was relieved by larger doses of Nisentil. In 13 per cent of the cases Nisentil alone was not sufficient and other supplementary agents were required to complete the cystoscopy.

The drug did not show any marked effect on the cardiovascular system; the blood pressure and pulse remained constant even in hypertensive subjects. However, respiration was markedly depressed, chiefly through a decrease in rate of respiration which may drop to 6 per minute for a brief period. This depression was greater with increasing amounts of Nisentil and with the presence of opiates. Sedation was variable. Side reactions appeared in 6 cases or 8 per cent: these included dizziness in 4, nausea and vomiting in 1, and Cheyne-Stokes respiration in 1. The incidence of side reaction was seen particularly in unpremedicated individuals.

Nisentil and Pentothal or Surital were administered to 38 cases in the series. Pentothal was given chiefly at the commencement of the procedure for the insertion of the cystoscope; subsequently the patient was drowsy or awake while the pyelograms were being taken. The amount of Pentothal used during the procedure was significantly less than in cases done with Pentothal alone (Table III). The average dose of Pentothal required with Nisentil was 260 mg. in males and 117 mg. in females, as compared to the amounts with Pentothal alone which were 711 mg. for males and 620 mg. for females. Patients anaesthetized with Nisentil and Pentothal were awake or responded to commands while those given

TABLE III

DOSAGE OF PENTOTHAL FOR CYSTOSCOPY

	Pentothal	
	Range	Average
Male	400 to 1200 mg.	711 mg.
Female	400 to 1000 mg.	620 mg.

	Nisentil–Pentothal	
	Range	Average
Male	50 to 675 mg.	260 mg.
Female	50 to 225 mg.	117 mg.

Pentothal alone were unconscious or slightly reactive at the end of the examination.

The main side reaction of this method was the marked depression of respiration when Nisentil was combined with Pentothal. Patients may have very slow respiration or complete apnoea with large doses or with rapid injection of Pentothal. If apnoea occurs gentle inflation of the lungs with oxygen will restore respiration in a few minutes.

In the third group of cases, where the combination of Nisentil, Pentothal and Nitrous Oxide was used, patients remained completely anaesthetized throughout the procedure. Here again the amount of Pentothal used was markedly reduced. Patients returned to consciousness rapidly at the end of the procedure. The chief side reaction here was again a brief period of respiratory depression.

DISCUSSION

The usefulness of Nisentil in cystoscopy has been assessed in this study. It has been found that successful cystoscopy and pyelography were carried out in 87 per cent of the cases without other supplementary agents. The drug has the property of brief duration of action so that the narcosis soon wears off after the examination. With this method the patient remains drowsy but awake so that he is able to co-operate and the pyelograms can be taken without any movement of the diaphragm. The respiratory depression is readily coped with by administering oxygen to the patient by mask. Oxygen should be given if there are any signs of respiratory depression especially in older individuals. Successful cystoscopy and pyelography can be carried out with this technique both in hospital and office practice if complete analgesia is not anticipated by the patient, since approximately two-fifths of the subjects may have slight discomfort from instrumentation. Nisentil alone is most suitable for the examination of female patients since 52 per cent suffered no pain. This is due to the fact that the female urethral is short and straight so that less analgesia is required.

Nisentil alone is not satisfactory if complete pain relief is contemplated by the patient because only 43 per cent (30 per cent male and 52 per cent female) have complete analgesia.

Nisentil in combination with Pentothal offers an alternative which is useful because it eliminates the discomfort of the insertion of the cystoscope and yet allows the patient to be sufficiently awake to co-operate during the pyelography. The initial injection of Pentothal is sufficient to relieve the initial discomfort while the Nisentil provides adequate analgesia when the cystoscope or ureteral catheters remain in the urethra. When Nisentil and Pentothal are used together competent personnel must be available to contend with the respiratory depression and apnoea which may occur. Usually a brief period of ventilation of the lungs with oxygen will restore adequate respiration. The advantage of the technique is that the amount of Pentothal is reduced significantly so that there are no prolonged after effects.

The combination of Nisentil, Pentothal, and Nitrous Oxide gives complete anaesthesia throughout the examination. The emergence from anaesthesia is rapid. The patient is usually awake before leaving the operating room. Here again apnoea may occur so that a competent anaesthesiologist should be present.

There were side reactions in 8 per cent of the cases, most of which were of minor nature. Dizziness, which was most common, was not seen in cases where there had been premedication with Demerol or morphine. Thus premedication not only reduces the incidence of side reactions but also reduces the anxiety of the patient, which is the prime purpose of the preoperative sedation. Finally, premedication reduces the amount of anaesthetic agent required during the anaesthetic.

Cystoscopy was used as a means to assess the analgesic action of Nisentil. Instrumentation of the urethra does not present a universally similar condition since there is a great variation between the male and female urethra. The female urethra is short and straight thereby requiring less analgesia. Even in the male urethra there is a wide variation in the degree of analgesia needed; obstruction to the bladder neck by the prostrate gland is common so that severe pain may be inflicted when the cystoscope is forced through the tight bladder neck. For these reasons we have found that there is a wide variation in the dosage of drugs required and the results produced by the drugs. Nisentil has been found to be a potent short-acting analgesic drug with marked depressing effect on respiration.

Summary

We have presented the results of a study of the analgesic effects of Nisentil in 135 urological cases. The cases were divided into three groups in which Nisentil was used alone, in combination with Pentothal or Surital, and in combination with Pentothal and Nitrous Oxide. Successful cystoscopy was carried out in 87 per cent of the cases where Nisentil was the sole agent. When Nisentil was combined with Pentothal the amount of the latter drug was significantly reduced. The side reactions and the limitations of the method are discussed. As with other potent analgesic agents, Nisentil had a marked depressing action on the respiration.

RÉSUMÉ

L'auteur présente les conclusions qu'il a tirées de l'étude des effets analgésiques du Nisentil dans 135 examens cystoscopiques.

Les cas furent divisés en trois groupes : le Nisentil étant utilisé seul, ou bien avec Pentothal ou Surital, ou encore, avec Pentothal et Protoxyde d'azote. Employé seul, le Nisentil permit une cystoscopie facile dans 87 pour cent des cas. Combiné au Pentothal, il fut possible de reduire de façon significative, la dose de ce dernier. Les réactions secondaires furent les étourdissements (4 cas), les nausées et vomissements (1 cas) et la respiration de Cheyne-Stokes (1 cas). Comme tous les autres analgésiques puissants, le Nisentil produisit une dépression marquée de la respiration.

REFERENCES

1. ZIERING, A., and LEE, J. Piperidine Derivatives: V. 1,3-dialkyl-4-aryl-4-acyloxypiperidines. J. Org. Chem. *12*: 911–914 (1947).
2. HOLLAND, H. L., and GROSS, E. G. Two New Analgesics. Federation Proc. 7: 227 (1948).
3. RANDALL, L. O., and LEHMANN, G. Pharmacological Studies on Analgesic Piperidine Derivatives. J. Pharmacol. & Exper. Therap. *93*: 314 (1948).
4. HAPKES, F. B., and BARNES, A. C. The Obstetric Use and Effect on Fetal Respirations of Nisentil. Am. J. Obst. & Gynec. *58*: 779 (1949).
5. SMITH, E. J., and NAGYFY, S. F. A Report on Comparative Studies of Newer Drugs used for Obstetrical Analgesia. Am. J. Obst. & Gynec. *58*: 695 (1949).
6. KANE, W. M. The Results of Nisentil in 1000 Obstetrical Cases. Am. J. Obst. & Gynec. *65*: 1020 (1953).
7. MCCREA, L. E., and POST, E. Use of Nisentil Hydrochloride as an Analgesic Agent during Cystoscopic Procedures. J. Internat. Coll. Surgeons *21*: 480 (1954).
8. EURICH, J. P. An Obstetrical Analgesia. Am. J. Obst. & Gynec. *69*: 124 (1955).

SINGLE INJECTION AND CONTINUOUS CATHETER PERIDURAL SEGMENTAL BLOCK ANAESTHESIA FOR GENERAL SURGERY*

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THE anatomy and contents of the peridural space (1) (2) and satisfactory methods of administering peridural segmental block anaesthesia have been adequately described in the literature (3). During the last few years the technique has been used in 1,236 surgical cases in the operating rooms of the Vancouver General Hospital. The anaesthetic drug used exclusively was 2 per cent xylocaine (lidocaine) in aqueous solution, or with adrenalin (1:300,000 or 1:200,000) added to lengthen the action of the drug: the needles found most satisfactory were No. 18 T with straight and huber points, manufactured by Becton, Dickinson & Company. On the basis of this clinical experience it is established that peridural segmental block anaesthesia deserves greater popularity among anaesthesiologists, and that it should have increasing importance in the armamentarium of those who use regional methods.

It is accepted that the technique is somewhat more difficult to master than others, and that induction of anaesthesia requires a longer period of time, but experience should minimize both of these problems. However, it is probably contraindicated when open reduction of fractures is to be undertaken, with the exception of Smith-Peterson nailing. The slight delay in onset of anaesthesia makes it possible to move the patient from bed to bell table before blood pressure changes occur. In addition, patients undergoing cystoscopy and transurethral resection should not have peridural anaesthesia unless the urologist is willing to wait until the anaesthesia is effective.

TABLE I

COMPLICATIONS (604 cases)

Failure or incomplete	13 (2.12%)
Lumbar puncture	6 (1.0%)
Needle in vein	1 (0.17%)
Atelectasis	1 (0.17%)
Sore back	2 (0.33%)

Table I illustrates the complications encountered in 604 consecutive cases.

Peridural segmental block anaesthesia has many advantages when used for surgical procedures below the diaphragm. These include its suitability for cardiac and poor risk cases (especially if prolonged surgical procedures are necessary);

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its freedom from post-anaesthetic sequellae; and its non-explosive character. It is suitable for outpatients, and single injections may be repeated without danger.

Dogliotti's "Loss of resistance" technique (4) (5) is the only satisfactory method of entering the peridural space with certainty, in the lower thoracic and lumbar regions. By this method a suitable needle is placed in the substance of the ligamentum flavum, its stylet is removed, and a 5 c.c. syringe filled with 2 per cent xylocaine solution is attached to its hub. Constant forceful pressure is then maintained on the plunger of the syringe as it is advanced slowly through the ligamentum flavum and until it passes through the periosteal layer of dura and enters the peridural space. At that moment resistance to injection of the solution will suddenly disappear, and the solution will flow rapidly into the peridural space. It is possible that the plunger of the syringe may stick in the barrel, and thus prevent transmission of the pressure change as the needle enters the peridural space. To make certain that this does not occur, a small bubble of air is allowed into the 5 c.c. testing syringe. Then increased pressure on the plunger will compress the bubble if the plunger is freely movable and the point of the needle is still in the ligamentum flavum.

First attempts at peridural puncture should be made at L 2-3 or L 3-4, allowing ample time for the technique, and the amount of anaesthetic drug injected into the peridural space should not exceed 10–15 c.c. (2% xylocaine). When sufficient skill and experience have been acquired, the peridural space may be entered at the optimum level and larger amounts of anaesthetic drug injected, up to 20 c.c.

All patients for upper abdominal surgery should have gastric suction started on the ward and should be sent to the operating room with a Levine tube in place. If doubt exists whether the patient's stomach is empty, then the patient should be kept awake during surgery or endotracheal intubation should be carried out.

An intravenous infusion should be started before or immediately after commencement of peridural anaesthesia. If the stomach is empty, pentothal 0.2 per cent added to the intravenous solution will prevent any possibility of drug reaction, and can be combined with nitrous oxide analgesia to keep the patient lightly asleep during surgery.

Frequently it is impossible to test levels of anaesthesia, or to keep the patient in an anaesthetic room until peridural block is complete. To avoid having a confused, struggling patient when surgical preparation is commenced, it is best to keep the patient either awake enough to co-operate, or asleep. In addition special care should be taken to ensure that leg restraints are properly applied, and that both arms are securely fastened. When surgical preparation and draping are complete the patient can be given light general anaesthesia.

Single injection peridural block has proven satisfactory for many surgical procedures below the diaphragm. These have included: all pelvic and gynaecological operations, rectal surgery, herniorrhaphy, lumbar sympathectomy, appendectomy, circumcision (adult), nephrectomy, nephrolithotomy, plastic surgery of kidney and ureters, all suprapubic urological procedures, laminectomy, spine fusion, excision of pilonidal sinus, ligation and stripping of varicose veins, mid thigh amputation, Smith-Peterson nailing of fractured femur, meniscectomy, and

exploration of the knee joint. Complications have been relatively few, and most of them have been due to inexperience.

Table II will serve as a guide for choosing injection sites.

TABLE II

SINGLE INJECTION SITES

Procedure	Site	Type of needle
Cholecystectomy Gastrectomy Perforated ulcer	T_{10-11} or T_{11-12}	Straight ↑
Kidney	T_{11-12}	Straight ↑
Abdomen Pelvis	T_{11-12} or T_{12}–L_1	Straight ↑
Hernia Lumbar sympathectomy	T_{12}–L_1	Straight ↑
Pilonidal sinus Fractured hip leg	L_{1-2} or L_{2-3}	Straight ↑
Laminectomy	Not at disc	Straight
Rectum Prostate Circumcision	L_{3-4} or L_{4-5}	Huber ↓

↑ Means that flow of solution is directed cephalad

↓ Means that flow of solution is directed caudad

Continuous catheter peridural segmental block may well prove to be the most satisfactory method of regional anaesthesia yet devised. An experienced anaesthesiologist can place a catheter with certainty in the peridural space at any desired level. Anaesthesia may be maintained during long surgical procedures, and post-operative pain control may be supplied in selected cases (6). This method has proved excellent for the following surgical procedures: gastrectomy, cholecystectomy and exploration of common duct, bilateral herniorrhaphy, ligation of inferior vena cava, bowel resection, and embolectomy. It may, however, be used in any surgical procedure in which the diagnosis is in doubt or which may require longer than 1½ hours.

Table III indicates the injection sites, and the catheter direction.

As yet, plastic tubing suitable for catheters is supplied only in rolls 100 feet long, which must be cut into 36″ lengths. When cut, the catheters are fitted with stylets made from No. 5 or No. 6 tonsil wire. The stylets should be about 40″ long, and must have the ends filed smooth so that they will not damage

TABLE III

CATHETER INJECTION SITES

Procedure	Site	Type of needle
Gastrectomy Gall bladder	T_{10-11} or T_{11-12}	Straight ↑
Bowel resection Ligate inf. vena cava Abdomen Pelvis	T_{11-12} or T_{12}–L_1	Straight ↑ or Huber ↑
Bilateral hernia legs	L_{2-3}	Huber ↑
Embolectomy	L_{2-3} or L_{3-4}	Huber ↑

the catheters. The prepared catheters should be wrapped separately, each with a catheter adapter, and autoclaved at 250° for five minutes.

Following placement of a needle in the peridural space, at the selected level, the stylet is withdrawn until it is about ½″ inside the catheter at one end (Figure 1). The needle is fixed and the catheter is gently inserted into the lumen of the needle, with its curve towards the direction it is to go in the peridural space. As the end of the catheter reaches the needle point–and the space–a characteristic resistance is always encountered, until the end of the catheter has

FIG. 1. Catheter about to be inserted into needle.

FIG. 2. Catheter in peridural space: stylet partly withdrawn.

passed into the peridural space. When the resistance ceases then the stillette should be withdrawn from the catheter as the catheter is advanced through the point of the needle (Figure 2). The catheter need only be advanced far enough into the peridural space to make certain that it will not be pulled out of the

FIG. 3. Catheter in position for taping.

FIG. 4. Catheter taped to patient's back.

FIG. 5. Patient in supine position. Catheter and loaded syringe shown.

space, as the needle is threaded backwards along the catheter. The catheter can then be taped to the patient's back, after the catheter adapter has been attached, and a test dose (2–3 c.c. 2 per cent xylocaine) can be given to rule out spinal. The patient is repositioned on the operating table, and if no anaesthesia is present within five minutes, a full dose of 15–20 c.c. of 2 per cent xylocaine is injected

into the catheter. This may be repeated at hourly intervals. Catheters should be removed before the patient leaves the operating room.

Vasopressor drugs are not administered in either single injection or continuous catheter peridural anaesthesia unless the systolic blood pressure falls below 80 mm. Hg., in normo-tensive patients, or unless the patient's condition requires careful regulation of the blood pressure. For this reason it is extremely important that blood pressures be taken at frequent intervals, especially immediately after peridural injections have been made. Age, site of injection of the anaesthetic drug, and amount injected will all tend to influence the blood pressure. Table IV for

TABLE IV

SINGLE INJECTION PERIDURALS

Age	No vasopressor	Vasopressor
10–19	16	—
20–29	29	3
30–39	29	15
40–49	24	15
50–59	11	21
60–69	16	19
70–79	8	33
80–89	3	12
90 +	—	1

single injection peridurals indicates that on the basis of age alone vasopressor drugs are unlikely to be required in patients under 30 years of age, and that a percentage of patients in all age groups will not need them. If hypotension does occur in healthy patients, owing to peridural segmental block, a minimum blood pressure of 80 mm. Hg. systolic is considered safe, and will produce a relatively bloodless operative field, with minimal blood loss.

Additional assistance in providing a bloodless field for surgery of the spine (laminectomy, spine fusion, and pilonidal sinus excision) may be provided by using 2 per cent xylocaine with adrenalin added (1:300,000 or 1:200,000) as the adrenalin produces a local vasoconstriction at the site of action.

Methedrine (Methamphetamine) and neosynephrine are the drugs of choice for maintenance of blood pressure. Methedrine is administered 5 mgm. intravenously and 15 mgm. intramuscularly to maintain blood pressure in poor risk cases, and frequently will raise the blood pressure to safe levels should serious hypotension occur. If more active control is necessary, 4 mgm. of neosynephrine may be added to 500 c.c. of intravenous solution, and the mixture used to maintain the blood pressure at satisfactory levels, by varying the speed of the intravenous drip. When blood pressure is difficult to maintain during surgery, it must be watched constantly until anaesthesia has worn off.

SUMMARY

Single injection and continuous catheter peridural segmental anaesthesia are satisfactory for most surgical procedures below the diaphragm. The continuous

catheter technique is limited in its use because of difficulty in preparing catheters, but should be more widely employed. Advantages, disadvantages, complications, and sites of injection are discussed.

RÉSUMÉ

Durant ces quelques dernières années, on a utilisé, dans les salles d'opération de l'Hôpital Général de Vancouver, le blocage anesthésique péridural segmentaire dans 1236 cas de chirurgie. En se basant sur cette expérience clinique, il est permis d'affirmer que l'anesthésie péridurale segmentaire mérite une plus grande popularité chez les anesthésistes.

Il est probable que cette technique est contre-indiquée dans les réductions ouvertes des fractures. En plus, on ne doit pas l'employer pour les cystoscopies ou les résections transurétérales à moins que l'urologiste est prêt à attendre le temps nécessaire à l'anesthésique pour être effectif.

Les complications presentées dans 604 cas sont analysées (Tableau I). La technique "par perte de résistance" de Doggliotti est la seule méthode satisfaisante d'entrée dans l'espace péridural. L'endroit d'élection pour injection unique de la solution anesthésique varie selon le niveau opératoire (Tableau II).

Quand on utilise un cathétère inséré dans l'espace péridural, l'anesthésie peut être maintenue pour de longues périodes de temps. Cette technique est décrite en détail et les points d'élection pour l'injection par cathétère dans diverses opérations sont donnés dans le tableau III.

On ne donne aucun vasoconstricteur chez les patients à tonus vasculaire normal à moins que la pression sanguine systolique tombe en bas de 80 mm Hg. En fait, la plupart des patients de moins de 30 ans ne réquièrent aucun vasoconstricteur.

REFERENCES

1. NETTER, FRANK H. The Ciba Collection of Medical Illustrations, vol. I (1953).
2. HALE, DONALD E., ed. Anesthesiology. Philadelphia: F. A. Davis Company (1954), p. 478.
3. BONICA, JOHN J. The Management of Pain. Lea & Febiger (1953), p. 512.
4. BROMAGE, P. R. Spinal Epidural Analgesia. E & S Livingstone, Ltd. (1954), p. 48.
5. MACMILLAN, ANGUS. Peridural Anaesthesia for Obstetrics. Canad. Anaes. Soc. J. *1*: 75 (1954).
6. CLELAND, J. G. P. Continuous Peridural and Caudal Block. Anesth. & Analg. *31*: 5 (1952).

ACUTE LARYNGOTRACHEOBRONCHITIS

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Acute laryngotracheobronchitis is a common disease which should be more widely understood. Invariably, it is associated with respiratory obstruction and frequently a tracheotomy under general anaesthesia is required. This paper deals with the disease from the viewpoint of the anaesthetist.

Acute laryngotracheobronchitis is an acute infective inflammation of the mucosa of the larynx, trachea, and bronchi. It is characterized by oedema of the larynx, toxaemia and a thick, viscid, non-membranous exudate in the tracheobronchial tree (1).

This disease affects children almost exclusively. The age incidence (2) ranges from three months to eight years, with 60 per cent of all cases occurring between one and three years of age.

The responsible organisms can be streptococci, either haemolytic or viridans, pneumococci, staphylococci, micrococci catarrhalis or haemophili influenzae. Predisposing factors include a low humidity usually associated with central heating, sudden environmental temperature changes, and possibly allergy.

Pathology

When the pathological features of this disease are perceived, its seriousness becomes obvious. Under normal conditions, the mucosa of the larynx and tracheobronchial tree is separated from the cartilage by an abundance of loose areolar tissue containing rich vascular and lymphatic plexuses. In addition, the glottic aperture of children is relatively small.

With the onset of infection in the upper respiratory tract, an intense inflammation of the mucosa and submucosa occurs. The associated swelling is not the usual "watery" oedema but consists of an acute inflammatory cell infiltration. A reduction of the lumen ensues throughout the respiratory tree but the earliest and most marked obstruction is in the larynx. The swollen inflammed larynx causes hypoxia and laryngospasm, which increases the vascular engorgement and oedema and a "vicious circle" results. Retained sticky secretions due to a diminished cough reflex augment the obstruction.

Within a few hours, laryngeal oedema can progress to complete closure of the glottis. Almost all deaths in this disease are the result of anoxia, either from acute asphyxia or from the effects of prolonged hypoxia.

Clinical Picture

The clinical picture varies with the severity of the infection and the degree of respiratory obstruction. Two forms of the disease are seen, the mild and the

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severe, but they differ only in degree. In a severe infection with marked obstruction, the following disturbances may be manifested:

1. *The central nervous system.* Cerebral signs are the most sensitive indicators of lack of oxygen. The child shows inattention, restlessness, and delirium which is the result of depression of the cerebral cortex by hypoxia and toxaemia. Occasionally convulsions occur which are associated with the high fever.

2. *The cardiovascular system.* The pulse rate is rapid owing to apprehension and fever combined with the reflex response to lack of oxygen and retention of carbon dioxide. Terminally, the pulse may become extremely fast and weak or else become very slow owing to direct anoxic depression of the cardiac muscle. The blood pressure may be normal or slightly elevated.

3. *The respiratory system.* Dyspnoea is the most prominent feature and may be inspiratory, expiratory, or both. The accessory muscles are working maximally and there is marked indrawing of the supraclavicular, suprasternal, and intercostal areas, and retraction of the lower sternum. Many children assume a "knee chest" position in an attempt to gain relief.

The respirations are shallow owing to the difficulty in inspiration and expiration. The rate is rapid owing to the stimulation of oxygen lack and excess carbon dioxide. Although a normal pulmonary minute volume may be maintained, the actual alveolar ventilation is quite inadequate.

4. *Integumentary system.* The skin is usually pale and occasionally ashen. Cyanosis of the finger nails and lips is common.

The combined effect of prolonged hypoxia, toxaemia, restlessness, and laboured respiration is extreme fatigue. The child may become too exhausted to maintain the fight for air and quickly sleep into death. Therefore, in the severe form of acute laryngotracheobronchitis, tracheotomy must be performed immediately.

Medical Treatment

Mild cases can be handled medically but since the disease can progress rapidly, constant competent observation is necessary during the acute phase. Mild cases are the most common and the following treatment is adequate.

1. A humid atmosphere is necessary. This can be achieved by placing the child in an oxygen tent fitted with a humidifier. The increased oxygen concentration helps to relieve the hypoxia and the high percentage of water vapour helps to prevent inspissation and retention of secretions.

2. Antibiotics must be administered promptly. Penicillin and streptomycin in the usual dosage are satisfactory.

3. Mild sedation is desirable. A short-acting barbiturate administered per rectum is valuable to allay apprehension and allow quieter and more efficient respirations.

Heavier sedation using large doses of barbiturate or opiates will mask the signs of progression of the disease. The central nervous system will be depressed, the respiratory effort weakened, the cough reflex depressed, and secretions will be retained. This may lead to bronchial obstruction associated with minimal signs of respiratory embarrassment, and quiet death may ensue. Atropine is contraindicated even if tracheotomy is contemplated as serous secretions are abolished.

Surgical Management

The evidence of progression of a mild case is shown by increasing restlessness, more laboured respirations, an increasing but weakening pulse which fails to respond to therapy, and diminishing air entry in the lung bases. Any one of these signs is an indication for a tracheotomy as soon as possible. Where reasonable doubt exists regarding the degree of respiratory obstruction, a tracheotomy should be performed.

In preparation for the operation, the child is placed on the operating room table and oxygen given during the draping. No anaesthetic should be administered at this stage, as even small amounts will produce either apnoea or laryngospasm. If an acute anoxic episode is added to a prolonged hypoxic period, death occurs promptly unless an airway is forced and artificial ventilation is carried out. It would be extremely difficult to pry open the mouth and force an endotracheal tube or even a Mosher tube through a tightly swollen larynx before the child was dead.

The method of choice is to open the child's mouth, insert a mouth gag, and pass a bronchoscope without any anaesthetic. A bronchoscope is most valuable because (*a*) it can be forced through the narrowed oedematous larynx, whereas an endotracheal tube would kink even with a stylet; (*b*) it establishes an airway which cannot be compressed; (*c*) it allows visualization of the trachea and bronchi and direct aspiration of secretions; (*d*) it allows the insufflation of oxygen. The lack of anaesthesia for insertion of the bronchoscope may seem to present difficulties but resistance is minimal, and on relief of the obstruction, the child immediately relaxes. A light ether oxygen anaesthesia is administered through the side arm of the bronchoscope. Only small quantities of the agent are necessary as the child is usually exhausted.

A tracheotomy (3) which is deliberate and unhurried can be carried out. A vertical midline incision in the lower neck is made, and using blunt dissection the trachea is exposed. The presence of a bronchoscope provides a rigid landmark and prevents injury to the oesophagus when the third and fourth tracheal rings are incised. The tracheotomy tube is gently inserted and the skin edges are loosely sutured.

Postoperatively the air entry in the lungs must be checked and then the child is returned to the humid atmosphere of his oxygen tent. Frequent aspiration of his respiratory tract through the tracheotomy tube should be carried out to prevent accumulation of secretions and bronchial obstruction. The tracheotomy tube is removed in four to seven days.

Complications

Serious complications are rare. If death occurs, however, it is usually the result of asphyxia. Any of the complications of an acute pyogenic infection can occur, such as endocarditis, meningitis, or septicaemia.

Pulmonary complications are commoner and may occur early or late. The early respiratory complications include pneumo-thorax, due to alveolar rupture from the high negative intrathoracic pressure consequent on excessive respiratory efforts. Occasionally, following relief of the obstruction, a temporary apnoea occurs. The

stimulation of respiration by oxygen lack and carbon dioxide excess is reduced and an interval is required for accommodation of the respiratory mechanisms to the new gaseous tensions of oxygen and carbon dioxide. Interstitial emphysema is common, usually the result of tight closure of the tracheotomy incision so that coughing forces air into the tissues.

Late pulmonary complications are usually the result of inadequate bronchial aspiration and include pneumonia, chronic bronchitis, lung abscess, and bronchiectasis.

Summary

The disease, acute laryngotracheobronchitis, is discussed from the viewpoint of the anaesthetist. The age incidence and aetiology are mentioned and the pathological changes leading to respiratory obstruction with its consequences are outlined.

The main clinical features of a fulminating case are described.

The treatment of the mild case is outlined; it should provide a humid atmosphere, antibiotic therapy, and mild sedation.

A severe case is treated, in addition, by early tracheotomy. The preoperative and surgical management is presented. The postoperative complications are summarized.

Résumé

L'auteur discute du point de vue anesthésique, la maladie appelée laryngotrachéobronchite aiguë. Il fait mention de l'étiologie et de l'incidence par rapport à l'âge de même qu'il décrit les changements pathologiques qui conduisent à l'obstruction respiratoire avec ses conséquences.

Les signes cliniques principaux d'un cas suraigu sont décrits.

Le traitement des cas bénins est donné. Il nécessite une atmosphère humide, les antibiotiques et l'emploie de légers sédatifs.

Un cas sévère nécessite en plus, au début, une trachéotomie. Les soins préopératoires et chirurgicaux sont présentés. Les complications postopératoires sont aussi données.

REFERENCES

1. Jackson, J. and Jackson, L. J. Bronchoesophagology. 1st ed., Philadelphia: Saunders (1950).
2. Turner, J. A. Present-day Aspects of Acute Laryngotracheitis. C.M.A.J. *70*: 401–4 (1954).
3. Fearon, Blair. The Role of the Otolaryngologist in the Management of Acute Laryngotracheitis. C.M.A.J. *71*: 482–4 (1954).

SUBGLOTTIC MEMBRANE: A CASE REPORT

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ENDOTRACHEAL intubation is today an accepted part of anaesthesia. Most complications following intubation are, in general, amenable to simple forms of treatment. For the more severe problems, amongst which is subglottic membrane, active diagnostic and therapeutic measures are required.

Aetiological factors responsible for complications of endotracheal intubation include infection, constitutional defects, tissue anoxia, local laryngo-tracheal abnormalities, shape, size and form of endotracheal tube, movement of tube in trachea, neck position, inflammation following duodenal catheter pressure with secondary involvement of trachea (1), trauma from the laryngoscope and the stylet, chemical irritants, following their use for sterilization of tubes (3), undue sensitivity of patient's trachea to endotracheal tubes, and allergic reactions (8).

It is an axiom that for the optimum treatment the exact diagnosis is necessary. To exemplify this and to indicate the necessity for a constant high suspicion of a subglottic membrane, the events leading up to such a case and a description of this case are here given.

During the middle of February, 1955, there was an unusual spate of post-operative respiratory complications in two of the hospitals in this area. These complications occurred at a time when there was a minor endemic of upper respiratory infections. One of the patients at the University Hospital, a white female, required an emergency tracheotomy following a cholecystectomy with a very tight fitting endotracheal tube. In retrospect this is considered to have been a case of subglottic membrane. The description of the investigated case follows.

M.S., a 68-year-old white woman, was admitted to the University Hospital for cholecystectomy on February 22, 1955. Cholelithiasis had been demonstrated radiologically two years previously, elsewhere. Since age 15 the patient had suffered from intermittent diarrhoea. In 1922 her only child was born. In 1927 hospitalization was necessary for several weeks for a nervous breakdown. In 1929 an uterine prolapse was repaired by an abdominal operation. A dilatation, curettage and insertion of radium for menopausal bleeding in 1938 was successful. All of these procedures were without complications. Since 1935 treatment for hypertension had been continuous.

Physical examination revealed a thin, poorly developed female, with a moist, pale skin. The pulse was 108, blood pressure 170/90, and respirations 22. The apical impulse was in the anterior axillary line. The abdomen was protuberant, with a midline infra-umbilical scar. The spine showed a mild kyphosis. The urinalysis, haematology, and blood chemistry were all within normal limits, except the serum amylase which was 320 Somogyi units (normal 50–200).

On February 24, 1955, a cholecystectomy was performed. Premedication consisted of demerol® 75 mgm. and atropine sulphate $\frac{1}{100}$ gr. Anaesthesia was

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induced with sodium pentothal®, anectine® and syncurine®. A No. 9 Magill portex tube, fitted with a low pressure, inflatable red rubber cuff, lubricated with tronothane® jelly was passed with difficulty into the trachea. An airtight fit between the trachea and the endotracheal tube was obtained without inflating the cuff. Anaesthesia was maintained with cyclopropane, diethyl ether, nitrous oxide, oxygen, and anectine®. Controlled respiration was employed for the major portion of the operation. The anaesthetic time was 2 hours 20 minutes. On extubation unusual resistance was encountered. Both the operation and the anaesthesia were uneventful. About 4 hours postoperatively the patient developed wheezing. At 10 P.M. that night the patient was in obvious respiratory embarrassment, with hoarseness, stridor, and tachypnoea. There was no pain. Pulse was 80 per minute, blood pressure 150/70, and respirations 28. The next morning her condition was certainly no better. A portable X-ray plate of the chest revealed no abnormality. A laryngoscopy, followed by a bronchoscopy, was performed. The epiglottic chink, the epiglottis, and the cords were only very mildly inflamed, but a greyish débris was found in the trachea below the cords at the level of the cricoid cartilage. This was removed with an immediate, impressive improvement in the patient's respiratory exchange and in her general condition. But this satisfactory state was not to continue. On February 26, 1955, the patient had resumed wheezing, hoarseness, trachypnoea, and stridor. A pharyngeal culture taken at this time showed "scant pus cells with a few Gram positive cocci. Culture revealed many staphylococcus aureus (haemolytic) sensitive to erythromycin® and chloromycetin®." On February 27, 1955, the patient was worse. There was marked stridor, cough, dyspnoea, tachypnoea, wheezing, and use of her accessory muscles of respiration. Pulse rate was 110 per minute, temperature 99.6, and respirations 28. On February 28, 1955, at 7:00 A.M. the patient was restless, confused, greyish-white in colour with cyanosed extremities and in an obviously dangerous condition. Temperature was 100.8, pulse 80, respirations 38. A No. 7 Magill portex endotracheal tube was passed with rapid improvement in respiration and colour. This procedure was followed by a bronchoscopy which showed a greyish-white membrane lying loose in the trachea below the cords, apparently loosened and displaced by the previous endotracheal tube. The membrane was removed. The cords appeared normal. The pathology report on the membrane was as follows: "The specimen consists of a portion of plastic appearing, grey material, which measures 1 cm. in diameter. Section shows a fragment of membranous tissue, consisting chiefly of fibrin, infiltrated by many collections of leukocytes, with polymorphonuclears predominating. Bacterial clumps are also noted towards the surface."

The subsequent progress of this patient was uneventful. Allergy skin tests for tronothane® jelly and red rubber performed during her convalescence were negative. The patient was ambulatory on March 1 and discharged from hospital on March 6, 1955.

Discussion

Subglottic membrane, also referred to as membranous laryngo-tracheitis (3)

and tracheal mucosa slough (2), occurs most frequently in poorly nourished females and in children (3, 7).

This complication may occur from a few hours to several days after operation, depending on the severity of the pathological changes occurring in the trachea. Four gradations, from a fibrinous membrane to an actual tracheal mucosa slough, have been described (3).

The obstruction occurs at the level of the cricoid cartilage. This is the most narrow portion of the trachea, unable to expand and covered by a sensitive loose areolar type of mucous membrane (4).

Postoperative complications of endotracheal intubation have a common entity of symptoms and signs. These include hoarseness, wheezing, stridor, cough, tachypnoea, dyspnoea, tachycardia, supraclavicular and sternal retraction. In many instances, a bronchoscopy is advisable to ascertain the exact condition. This is mandatory if a subglottic membrane is to be diagnosed correctly. It will then be found that the laryngeal anatomy is practically unchanged up to the cricoid cartilage where the membrane will be encountered. Removal of this membrane will relieve the obstruction. Repeated bronchoscopy may be necessary in some instances, as the membrane may recur. Impediment to the respiration is partly due to the obstructive débris and partly to the reflex adduction of the cords due to irritation from the membrane (4).

It must be evident that a number of subglottic membranes could be missed, either when the patient coughs up the membrane, as might be the case in an healthy male or when a tracheotomy is performed to alleviate a severe obstruction without a preliminary laryngoscopy to rule out laryngeal oedema. Occasionally, despite repeated bronchoscopies, a tracheotomy is required as a life-saving measure. Particularly is this the case in children (7).

It would appear that minor trauma, associated with low grade infection, is the main factor contributing to the formation of a subglottic membrane (3).

It is noted that the longer the endotracheal tube is in position, the greater is the possibility of postoperative complications (1).

Preventive Measures

At times of prevalent respiratory infections, limit the use of endotracheal tubes to cases where it is absolutely necessary, particularly avoiding cuffs where possible; employ throat packs in preference.

Arrange for physiotherapy as a routine.

Employ antibiotics where indicated.

Avoid movement of the tube in the trachea with correct taping or by employing a fixing apparatus, such as a divided airway or an Artusio bite block.

Avoid hyperextension of the neck, particularly in children.

Avoid sterilization of tubes with chemical irritants. Employ clean tubes, and those that will mould to the anatomy of the patient.

Use the laryngoscope and stylet with skill.

Select a satisfactory size of tube.

Obtain a satisfactory nutritional state of the patient.

Conclusion

Although postoperative complications of endotracheal intubation cannot be entirely avoided, they can be minimized by constant care and vigilance. Particularly, the patient can be saved the psychic trauma of a tracheotomy by the early diagnosis of a subglottic membrane.

Summary

A case of subglottic membrane is described in an elderly white female following a cholecystectomy with an oversized cuffed endotracheal tube. The need for accurate diagnosis and the danger of being satisfied with a single bronchoscopy is pointed out. Aetiological factors and preventive measures are outlined.

Résumé

L'étiologie des complications de l'intubation endotrachéale comprend le trauma, l'infection, les déficiences constitutionnelles et l'allergie.

Une femme agée, de race blanche à nutrition déficiente, chez qui l'on avait utilisé un gros tube endotrachéal à manchon durant une cholécystectomie, développa une membrane sous glottique. Ces membranes se forment au niveau du cartilage cricoide et nécessitent un diagnostic bronchoscopique. En les enlevant on guérit l'obstruction respiratoire.

Pour les prévenir on doit user d'habilité et d'attention. Le tube choisi doit être de calibre satisfaisant, fabriqué de matériel qui peut s'adapter à l'anatomie du patient. Les tubes doivent être propres cependant il ne faut pas les stériliser par des irritants chimiques. Le tube doit rester immobile dans la trachée. Les femmes à nutrition déficiente et aussi les enfants sont les patients les plus susceptibles de souffrir de cette complication.

REFERENCES

1. Dwyer, C. S., Kronenberg, S., and Saklad, M. The Endotracheal Tube: A Consideration of its Traumatic Effects with a Suggestion for the Modification thereof. Anesthesiology *10*: 714 (1949).
2. Turner, F. L. Sloughs of the Tracheal Mucosa. Lancet 2: 237 (1949).
3. Muir, A. P. and Straton, J. Membranous Laryngo-Tracheitis following Endotracheal Intubation. Anaesthesia 9: 105 (1954).
4. Etsten, B. and Mahler, D. Subglottic Membrane: A Complication of Endotracheal Intubation. New England J. Med. *245*: 957 (1951).
5. Guedel, A. E. and Waters, R. M. Endotracheal Anaesthesia: A New Technique. Ann. Otol. Rhin. & Laryn. *40*: 1139 (1931).
6. Snyder, J. J. and Gants, R. T. Respiratory Obstruction at the Glottic Level. Anaesthesiology *14*: 195 (1953).
7. Feinmesser, M., Aladjemoff, L. and Chayen, M. S. Some Laryngotracheal Complications associated with Endotracheal Anaesthesia. Arch. Otolaryng. 59: 555 (1954).
8. Lundy, J. S. Clinical Anaesthesia. 1st ed., Philadelphia: W. B. Saunders (1942).

CORTISONE AND ANAESTHESIA

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In 1855 Dr. Thomas Addison published a monograph entitled "The Constitutional and Local Effect of Disease of the Suprarenal Capsules." This is the first study of great value in the history of endocrinology of the Adrenal Glands. He stated that these glands are essential for the maintenance of life.

In 1856 Brown-Séquard performed the first experimental adrenalectomy to confirm the statements of Addison. But it was not until 1930 that we were sure of the hypophyseal control of the adrenals and we began to extract biologically active substances from these glands.

Only a few years ago science was successful in isolating Cortisone and A.C.T.H. An average of nearly two thousand papers have since been published every year on these hormones. It is easy to imagine how chaotic and contrasting are many of their findings.

A.C.T.H. is a polypeptide and its formation may be influenced by the diet: high carbohydrate and low protein intake may decrease the output, severe denutrition produces a syndrome in many ways similar to hypophysectomy. This hormone is secreted by the basophil cells in the pituitary gland and the secretion seems to be regulated both by nervous impulses from the hypothalamus and by chemical substances reaching the gland through the hypophyseal portal system of blood vessels from the hypothalamus to the anterior lobe. The amount of cortical hormone in the circulation also influences the production. Besides there is a theory, now denied by some authors, that postulates adrenalin and noradrenalin as important factors in the stimulation of A.C.T.H. output.

Cortisone (11-dehydro-17-hydroxycorticosterone) is released by the adrenal cortex and A.C.T.H. is the most important stimulus. M. Saffran and coworkers (1) found that homogenated hypothalmic tissue stimulates isolated adrenals only after adding adrenalin or noradrenalin. These two compounds alone have no action on the isolated adrenals. A substance extracted from an impure vasopressin preparation has the same potency as the one found in the hypothalamic tissue. It strongly stimulates the isolated adrenals in presence of adrenalin and noradrenalin. The chemical structure is still unknown, but there is evidence to believe that it is a peptide. In addition the level of circulating cortisone regulates the cells of the adrenal cortex in the formation of the hormone itself. Other endocrine glands may be responsible too.

The interrelationship of the pituitary-adrenal system and other endocrine systems is so wide and complicated and still so much in the dark that it is beyond the scope of this paper to go into it.

In brief I shall now enumerate the actions that the A.C.T.H.-Cortisone combination seems to have on the organism. In this I shall follow Professor Li

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(1950) (2), Sprague (3), Power and Mason (1950), Suzman (1953) (4), and other authors (24, 25).

1. Retardation of body growth and antagonism to the action of the growth hormone. This demands the careful adjustment of dosage in infants and children.

2. Increase in nitrogen and potassium excretion. Signs of hypopotassaemia may occur, such as apathy, lethargy, muscular weakness, cramps, abdominal pain, and distension. This complication can be corrected or controlled by the administration of adequate amounts of KCl.

3. Increase of the free aminoacid content of the plasma.

4. Glycosuria and hyperglycaemia. This can be disregarded unless the patient is diabetic, in which case extra insulin must be given.

5. Increase of body fats.

6. Hypertrophy of the liver with increased hepatic blood flow and increased liver fats. Aterman (1953) (5) showed that in rats Cortisone decreases the liver resistance to toxic substances, such as CCl_4.

7. Increase of Ketone bodies in urine and blood.

8. Diminution of the plasma alkaline-phosphatase.

9. Deterioration in chondriogenesis and osteogenesis of the tibia. Tissue wasting and osteoporosis are more apt to occur in elderly patients, in whom spontaneous fractures have been reported. To prevent or control these complications high protein diet, calcium, and anabolic agents, such as androgens and estrogens, should be administered.

10. Thinning of the epidermis and atrophy of the sebaceous glands and the growing parts of the hair.

11. Corticogenic hypothyroidism. This syndrome can develop only with prolonged administration, but the complication is of the greatest importance, because lack of thyroid hormone diminishes the responsiveness of the adrenal cortex to A.C.T.H. and of the tissues to Cortisone, with the result that the administration may become ineffective.

12. Involution of the thymus and lymph-nodes with depletion and involution of lymphocytes.

13. Decrease in circulating eosinophils, but increase in the production of neutrophils and erythrocytes.

14. Enhancement of work performance, because of augmentation of muscular power.

15. Improved resistance in normal rats to cold, starvation, and low atmospheric pressure.

16. Increased capillary resistance.

17. Inhibition of the insulin effect on isolated diaphragm of normal rats, but not of hypophysectomized animals.

18. Inhibition of male accessories of normal rats, but not of hypophysectomized animals.

19. Early retention of NaCl and H_2O, followed by increased excretion while the hormone is still being administered. This early retention may be very harmful for certain patients, such as those affected by heart diseases or hypertension, and during pregnancy. However, this complication can be controlled by decreasing the NaCl intake and by prescribing substantial amounts of KCl, which tends to

limit the retention of NaCl and H_2O; mercurial diuretics and cation exchange resins may also be of value.

20. A.C.T.H. stimulates the adrenal cortex output of steroids. Morphologically there is hypertrophy and hyperplasia, involving mainly the zona fasciculata and the zona reticularis, with narrowing of the zona glomerulosa. The secretory activity is increased and there is depletion of cell lipids.

21. Cortisone produces exactly the reverse of effects seen in unilateral hyperfunctioning cortical tumours. The evidence for this statement is: (*a*) postcortisone asthenia, (*b*) depression of urinary 17-ketosteroids during and after administration, (*c*) diminished response to A.C.T.H. (Thorn's Test), (*d*) atrophy of various degrees of the adrenal cortex observed at necropsy.

22. A.C.T.H. and Cortisone have been seen to produce some androgenic changes in children and young women, such as acne, hirsutism, moonlike face, buffalo hump, atrophic striae and thinning of the scalp hair, which have immediately regressed when the administration of the drug was stopped.

23. Menstrual function is usually stopped, especially in young girls.

24. A wide variety of psychic effects has been reported by many. Mild degrees of stimulation and euphoria are fairly frequent. Maniac behaviour, depression, and frankly psychotic states are indeed more rare. Severe reactions are more likely to occur in persons with a background of nervous instability.

25. A.C.T.H. and adrenocortical steroids, by this complex and wide variety of actions, have a great influence on the defence mechanisms of the body against stress. In this sense they constitute a basic factor in the general adaptation syndrome and the stress theory of disease propounded by Selye (23). They increase the defence mechanism of the host rather than attack the pathogen, irrespective of its nature. It is therefore understandable that we may now meet with success even when the cause of the disease is unknown. They are natural biological products and, although their influence on the body is often very profound, their action is nevertheless physiological in type as they produce an exaggeration or a diminution of normal metabolic processes. Thus no ill effect of permanent nature has ever been observed in patients who have received these hormones continuously for long periods. Most of the side effects and complications have occurred only during high dosage administration, and in children and young adults.

26. Winter and Flataker (1953) (6) found that in animals under the effect of morphine, cortisone has a definite central stimulating action influencing the entire cerebrospinal axis.

27. The oxygen consumption in granulation tissue is 66 per cent decreased by Cortisone.

28. Abrams and Harris (1951) (7) found that in rabbits treated with Cortisone there was a marked and immediate increase in the amplitude of the QRS deflections and T-waves. However, Chapman (26) and coworkers demonstrated in dogs that this hormone had no deleterious effects on the infarction areas, and the healing process was not at all impaired.

29. Kenyon (1947) (8) has pointed out that certain signs and symptoms of adrenal tumours have been reproduced to some extent by the administration of pure steroids: (*a*) hypertension by Desoxycorticosterone Acetate; (*b*) Na^+ and

H_2O retention by Desoxycorticosterone Acetate and Cortisone; (*c*) diabetes and N_2 loss by Cortisone; (*d*) N_2 gain and somatic growth by testosterone (one should also keep in mind the work of Kinsell (1952) (9) who reported that the catabolic effects of Cortisone on proteins are neutralized by testosterone); (*e*) masculinization and feminization with depression of gonadal function by androgens and estrogens respectively; (*f*) atrophy of the adrenal cortex by Cortisone.

Cortisone and Anaesthesia

I shall only examine those situations in which Cortisone directly concerns the anaesthetist, and this is around the date of an operation. He will find it indicated: (1) To prepare the patient for an operation treating conditions not directly involving the adrenal cortex; (2) To prevent shock and speed recovery; (3) To prepare the patient for adrenocortical surgery.

1. Cortisone ameliorates bronchial asthma as proved now by many workers. Therefore it can be administered for this purpose to severely affected patients pre-operatively. The mechanism of action seems to be due to the antihyaluronidase effect. But it must be remembered that it has been found that rheumatoid arthritic patients have a consistent decrease in functional residual capacity of the lung, paralleling the increase in skeletal mobility.

MacGougan and Thorson (1952) (10) found A.C.T.H. very useful in relieving oedema and bronchial hypersecretion, before bronchoscopy for the removal of foreign bodies.

Margulis (11) in 1951 and Fleishman (12) in 1953 reported cases of post-traumatic anuria which responded dramatically to A.C.T.H. and Cortisone. The mechanism of action is obscure, but seems to be the result of the fact that these hormones are able to relieve the post-traumatic ischemia of the kidney.

Horwitz (1953) (13) used Cortisone very successfully to relieve the severe bronchospasm in a bad case of bronchiectasis in order to perform a lobectomy.

Suzman (1953) (4) administered A.C.T.H. to three patients in severe shock caused by pulmonary emboli, who were not responding at all to anti-coagulant therapy. Prompt and dramatic improvement ensued and recovery occurred. The fourth patient improved, but died later.

Lurie (1953) (14) treated a man in barbiturate coma with 20 mg. of Cortisone and Vitamin B_{12} in 1,000 cc. of normal saline with return of consciousness in a few hours. However Gorby (1953) (22) showed that the protective effect of Cortisone against pentobarbital LD_{50} is minimal.

2. Cortisone (Li, 1950 (2)) by its complex mechanism of action increases the resistance to stress stimuli, if administered preoperatively; but Modern (1951) (15) advises caution and even says that patients on Cortisone should be taken off, because it may delay healing owing to the tissue-repair inhibiting effect. However, it is now generally agreed that moderate doses do not impair healing or body resistance to infection, and that patients on Cortisone therapy can safely undergo surgery as long as the dosage is increased for a few days around the time of the operation.

Very debilitated, cachectic, and senile patients and those who have suffered severe and prolonged stress would have the Thorn's Test, the Epinephrine-

Eosinophil Test, and the Eosinophil count done to assess as much as possible the Adenohypophysal-Adrenocortical Reserves. Hayes and Coller (17), Kelso and Keaty (18), and many others fully support this view and state that almost miraculous results can be achieved with the administration of small amounts of Cortisone before and after operation, according to the case.

Patients who have had Cortisone for any length of time must be presumed to have some atrophy of the adrenal cortex, which may produce varying degrees of cortical insufficiency when under stress such as surgery, fever, and anaesthesia (Sprague (3), Power and Mason 1950, Paulshock 1954 (19)). Sudden and dangerous hypotension may develop and may not respond to palliative treatment. Cortisone is the specific remedy, if given in time, and there is no better time than before the crisis develops.

3. Walters and Kepler (20) say that the most important factor in surgical therapy is the anticipation, prevention, and control of postoperative adrenocortical insufficiency.

Now that Cortisone and Desoxycorticosterone Acetate (DOCA) are available in pure form and patients without adrenal glands can be kept in good health for long periods, it is our duty to see that adrenal crises are prevented.

Until the last decade the mortality from the estirpation of hyperfunctioning adrenal tumours was very high and Cecil (21) reports 33 per cent deaths. An

TABLE I

SUBSTITUTION THERAPY FOR TOTAL ADRENALECTOMY
(Huggins and Bergenstal 1951 (16))

On day before the operation		
Cortisone	50 mg. I.M.	Every 6 hours
Desoxycorticosterone Acetate	5 mg. I.M.	Once a day—6 a.m.
NaCl	5 gm. orally	Once a day—6 p.m.
Operation day		
Cortisone	150 mg. I.M.	At 7 a.m.
Desoxycorticosterone Acetate	5 mg. I.M.	At 7 a.m.
Operation		At 8 a.m.
Cortisone	50 mg. I.M.	Every 4 hours
First postoperative day		
Cortisone	50 mg. I.M.	Every 6 hours
Desoxycorticosterone Acetate	5 mg. I.M.	Once
NaCl	3 gm. orally	
Second postoperative day		
Cortisone	50 mg. I.M.	Every 12 hours
Desoxycorticosterone Acetate	0–3 mg. I.M.	Once
NaCl	3 gm. orally	

During the subsequent days the dose of steroids is gradually reduced until the sustaining dose of Cortisone is reached (25–50 mg. daily) about one week after the operation. Desoxycorticosterone Acetate is usually not required for maintenance therapy.

important finding, in patients who died for the removal of an adrenal tumour, was that the controlateral adrenal gland could not be found at autopsy.

Adrenocortical insufficiency is rarely cured once it has developed immediately after an operation, especially if it is at all severe. The rule must be to treat the patient in advance as if the insufficiency were certain to develop postoperatively, and to withdraw the essential medicines slowly in the days following the operation. Therefore the well-timed administration of adequate doses of Cortisone and Desoxycorticosterone Acetate is most important. (See Table I.)

Blood loss must be replaced by transfusion during and after the operation, if necessary. The systolic blood pressure must be maintained above 100 mm. Hg. using continuous infusion of Noradrenalin 10 y/cc. of N.S.S. if required. The total amount of the fluid injected during the first postoperative day should not exceed 1,500 cc. If the temperature rises above 38°C., 0.6 gm. of Acetylsalicylic acid is given orally. The maintenance dose of Cortisone 25–50 mg. daily is usually started on the sixth postoperative day. The patient supplements his diet by ingesting 2–4 gm. of NaCl daily.

Conclusion

Today Cortisone permits the surgeon and the anaesthetist to perform operations to cure diseases which only a few years ago were extremely dangerous. The surgical approach may then have been worse than the disease itself to the patient, and very discouraging indeed to the surgical team. Now adrenal surgery can safely be performed and the anaesthetist has at hand a drug that allows him to bring through an operation many patients whose general condition might, before, have been an absolute contraindication to surgery and anaesthesia. Nevertheless, we must not forget that many other problems have been created by Cortisone, because there is no tissue or system in the body which is not influenced in its metabolism by the A.C.T.H.-Cortisone combination. Up to date we have only a fragmentary knowledge of its mode of action, and I believe that this should be a stimulus to use the greatest caution, both in its clinical application and in the interpretation of its effects.

Summary

Cortisone and A.C.T.H. act on every tissue of the organism by a mechanism which is still unknown; therefore, they must be used with extreme care. The cases must be meticulously selected and the dose must be adjusted for each case so that it will bring about the best result with the least side effects. The evaluation of these results is also difficult.

On the whole, we feel that it is better to use A.C.T.H. than Cortisone, because in this way at least the post-cortisone hypotrophia and hypoplasia of the adrenal glands, so dangerous to "stress," can be completely avoided.

The treatment for patients undergoing adrenal surgery is outlined.

Résumé

La Cortisone et l'A.C.T.H. agissent sur tous les tissus de l'organisme par un mécanisme encore inconnu. C'est pourquoi, on doit les employer qu'avec très

grandes précautions. Les cas doivent être choisis de façon méticuleuse et la dose doit être ajustée pour chaque cas de tel sorte qu'elle produise le meilleur résultat possible avec le moins d'effets secondaires. L'évaluation des résultats est aussi difficile.

A tout considérer, nous croyons qu'il vaut mieux employer l'A.C.T.H. que la Cortisone parce que de cette façon au moins, on évite les effets d'hypotrophie et d'hypoplasie des surrénales si dangereuses sous le "stress."

On donne le traitement à suivre chez les patients qui doivent avoir une intervention sur les surrénales.

REFERENCES

1. Saffran, M. *et al.* Production of Corticosteroids by Rat Adrenals *in vitro*. Endocrinology *50*: 639 (1952).
   Schally, A. V. Endocrinology (in press 1955).
   Schally, A. V. and Benfey, B. G. Role of the Neurohypophysis in the Release of A.C.T.H. Meeting of the American Endocrine Society, Atlantic City, June, 1955. Personal Communication.
2. Li, C. H. Action of A.C.T.H. Lancet *1*: 213 (1950).
3. Sprague, R. G. *et al.* The Physiological Effects of Cortisone and A.C.T.H. in Man. J.A.M.A. *144*: 1341 (1950).
4. Suzman, M. M. Clinical Application of Corticotropin and Cortisone Therapy. South African Med. J. 27: 195 (1953).
5. Aterman, K. and Ahmad, N. D. Cortisone and Liver Function. Lancet *1*(2): 71 (1953).
6. Winter, C. A. and Flataker, L. Effects of Cortisone, Desoxycorticosterone, Ashenscorticotropic Hormone and Diphenhydramine upon the Response of Albino Mice to General Anaesthetics. J. Pharmacol. & Exper. Ther. *105*: 358 (1952).
7. Abrams, W. B. and Harris, T. N. Effects of Cortisone on E.C.G. of Normal Rabbits. Am. Heart J. *42*: 875 (1951).
8. Kenyon, A. T. Adrenal Cortical Tumors. Physiologic Considerations; in Endocrinology of Neoplastic Diseases. Twombly and Pack, editors. New York: Oxford University Press (1947).
9. Kinsell, L. W. *et al.* Dietary Modifications of Metabolism and Clinical Effects of A.C.T.H. and Cortisone. Ann. Int. Med. 37: 921 (1952).
10. MacGougan, M. K. and Thorson, S. B. A.C.T.H. in Aspiration of Peanuts. C.M.A.J. *66*: 371 (1952).
11. Margulis, R. R. in Mote, J. R. Second Clinical A.C.T.H. Conference. London: Churchill Limited (1951).
12. Fleishman, S. J. Prompt Reversal of the Post-Traumatic Oliguric Syndrome by A.C.T.H. and Cortisone. South African Med. J. 27: 234 (1953).
13. Horwitz, M. Bronchial Asthma, Rheumatoid Arthritis and Connective Tissue Diseases: Treatment with Cortisone and A.C.T.H. South African Med. J. 27: 213 (1953).
14. Lurie, M. B. Treatment of Barbiturate Poisoning with A.C.T.H. Acta Med. Or. (Jerusalem) *12*: 87 (1953).
15. Modern, F. W. A.C.T.H. and Cortisone in Surgery. Ann. West. Med. & Surg. *5*: 153 (1951).
16. Huggins, C. and Bergenstal, D. M. Surgery of the Adrenals. J.A.M.A. *147*: 101 (1951).
17. Hayes, M. A. and Coller, F. A. Neuroendocrine Control of Water and Electrolyte Excretion during Surgical Anaesthesia. Surg., Gynec. & Obst. *95*: 142 (1952).
18. Kelso, W. and Keaty, C. Postoperative Use of Cortisone. Surg. Gynec. & Obst. *92*: 295 (1951).
19. Paulshock, B. Z. Surgically Precipitated Adrenal Cortical Insufficiency in a Patient Previously Receiving Cortisone. Delaware State M. J. *25*: 15 (1954).

20. WALTERS, W. and KEPLER, E. J. Surgical Lesions of the Adrenal Glands. J.A.M.A. *111*: 1051 (1938).
21. CECIL, H. L. Hypertension, Obesity, Virilism and Pseudohermaphroditism as caused by Suprarenal Tumors. J.A.M.A. *100*: 463 (1933).
22. GORBY, C.K. *et al.* The Effects of Cortisone and Desoxycorticosterone on the Toxicity of Barbiturates. J. Am. Pharm. A. (Scient. Ed.) *42*: 213 (1953).
23. SELYE, H. A Syndrome Produced by Diverse Noxious Agents. Nature (London) *138*: 32 (1935).
——— The General Adaptation Syndrome and the Diseases of Adaptation. J. Clin. Endocrinol. *5*: 117 (1945).
24. MOORE, F. D. and BALL, M. R. The Metabolic Response to Surgery. 1st ed., Springfield, Illinois: Thomas (1952).
25. DRILL, V. A. Pharmacology in Medicine. 1st ed., New York: McGraw-Hill Book Company, Inc. (1954).
26. CHAPMAN, D. W. *et al.* Effects of Cortisone in Experimental Myocardial Infarction. Am. J. Med. Scien. 223: 41 (1952).

PROLONGED DURATION OF APNOEA DUE TO SUCCINYLCHOLINE

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IN 1949 Bovet and his colleagues (1) described the paralysing action of the bis-choline esters of succinic acid, showing that they produced rapid paralysis of short duration. Concurrently Bovet-Nitti (2) showed that the destruction of these compounds in the blood was due to enzymatic hydrolysis. Evans, Gray, Lehmann and Silk (3) further demonstrated that the pseudo-cholinesterase of the serum was chiefly responsible for the hydrolysis, the true cholinesterase of the cells having little effect.

The stages in the breakdown are first, hydrolysis at a fairly rapid rate to succinylcholine and choline, and then hydrolysis of succinylmoncholine more slowly to succinic acid and choline, less than 3 per cent being excreted unchanged in the urine (4). This breakdown usually occurs in three to five minutes, but numerous case reports of prolonged duration have appeared in the literature (5–11).

Scoline® (succinylcholine chloride dihydrate) was the brand used in the following two instances of prolonged apnoea.

Case 1

H.B. A 70-year-old woman was admitted with large bowel obstruction. When presented for operation she was adequately hydrated, her B.P. was 120/80 and she was in a reasonably fit condition.

Morphia gr. $\frac{1}{6}$ and atropine gr. $\frac{1}{100}$ were given one hour before operation.

Induction was with Thiopentone 250 mg. and Scoline® 50 mg. A No. 8 Magill's cuffed catheter was passed and respirations recommenced in four minutes. Maintenance was with 6 litres nitrous oxide and 2 litres oxygen. An intravenous infusion of Scoline® 0.1 per cent was commenced (12).

The total operating time was two hours, during which a short circuit anastomosis was performed for carcinoma of the colon. Secondaries were present in the liver. Up to the time of commencement of closure of the peritoneum, periods of spontaneous respirations were permitted and adequately assisted where necessary. In all 500 mg. of Scoline® were used. As relaxation for closure of the peritoneum was inadequate, 50 mg. of Scoline® were given from a syringe. The operation was completed twenty minutes later, but apnoea still persisted. There were, however, very tiny movements of the rebreathing bag.

Nikethamide 10 cc. was given without effect; in fact the faint movements of the rebreathing bag disappeared.

Controlled respiration was carried out using 100 per cent oxygen for periods up to ten minutes, and both hypo- and hyperventilation were tried without success.

Respirations gradually began to return $1\frac{3}{4}$ hours from the time when the last dose of Scoline® had been administered, but it was three-quarters of an hour

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later before tidal exchange was adequate. Consciousness began to return shortly before this.

At no time did her condition give rise to any anxiety.

Postoperatively the following were her cholinesterase estimations (Warburg): serum cholinesterase–120, red cell cholinesterase–96. The serum potassium was not estimated.

Case 2

C.P. A young married girl age 23 years was presented for oesophagoscopy. Before operation nothing abnormal was found. Premedication was morphia gr. $\frac{1}{6}$ and atropine gr. $\frac{1}{100}$, 1 hour before.

She was induced with 500 mg. of Thiopentone and 50 mg. of Scoline®. Intubation was carried out and maintenance was nitrous oxide and oxygen 6/2 litres. The procedure took fifteen minutes to complete but she was still apnoeic at the end of this time.

Nikethamide 5 cc. was given and repeated a few minutes later. Again the impression was gained that she became even more flaccid than before.

Hyper- and hypoventilation were again tried without success. Oxygen 100 per cent was given for some periods.

In all the apnoea persisted for $2\frac{1}{2}$ hours and again the onset of consciousness almost coincided with adequate tidal exchange. Respirations had gradually commenced about three-quarters of an hour before they became adequate for oxygenation.

The cholinesterase estimations were: serum–37, red cell–not estimated.

In contrast to these two cases the following is the history of a case in which it was expected that a prolonged recovery time would result from succinylcholine, but in fact did not occur.

Case 3

F.L. A man 48 years of age suffering from acute liver failure with gross ascites developed an acute abdomen. It was at once realized that owing to the hepatic condition his serum cholinesterase should be low (13). In fact a blood sample before operation showed it to be 44. Accordingly it was decided to use Scoline® to try his sensitivity to the drug.

Induction was with Thiopentone 200 mg. and Scoline® 25 mg. Spontaneous respirations commenced in five minutes and an intravenous infusion of 0.1 per cent Scoline® was commenced. Maintenance was with nitrous oxide and oxygen 6/2 litres. The operation lasted $\frac{1}{2}$ hour, during which time a gangrenous appendix was removed. In all 150 mg. of Scoline® were used and spontaneous respirations were present at the end of the procedure.

His postoperative cholinesterase estimations were: serum–44, red cells–106.

Discussion

It would appear from the experience gained from the above cases that a low serum cholinesterase is not the only factor in patients who show a prolonged effect from succinylcholine. The low value was present in cases 2 and 3, but in

one the response was normal and in the other abnormal. Case 1 showed an abnormal response with a normal level of serum cholinesterase.

Many factors have been blamed for the prolonged apnoea due to succinylcholine, among them hyperventilation (14), an alteration of the patient's ph (10), persistent effect of thiopentone (8), overdosage (18) etc. Evans *et al.* (17) are quite definite that the low serum cholinesterase level is enough to explain the prolonged recovery time. They, and Bourne, Somers and Collier (16) between them have had eight cases of somewhat prolonged apnoeas and in each one the serum cholinesterase was low. Lehmann (13) goes so far as to state that "to produce dramatic delay in recovery the enzyme level must obviously be very low." Evans *et al.*, however, had two further instances which they could not explain by low serum cholinesterase value. In these they suggested a low serum potassium as being a possible causal factor.

That a low serum cholinesterase level is a factor is undoubtedly true, but I am convinced that there must be others, which in the present state of our knowledge are not yet apparent.

In my opinion it is quite possible that where the patient responds with an apnoea of abnormal duration, succinylcholine or its breakdown products may exert a central as well as a peripheral effect. I am prompted to this conclusion by the delay in the return to consciousness until the return of respirations, despite the administrations of 100 per cent oxygen. Others have reported similarly.

Methods of Treatment

Presuming that the delay in recovery is caused by a low level of serum cholinesterase, then the rational treatment is the raising of this level, either by intravenous injections of concentrated serum cholinesterase or by fresh blood transfusions. Dramatic results have been claimed for the transfusions of fresh blood (5) (6), but this may not be readily available in many hospitals, and the apnoea may well have terminated by the time a supply becomes available.

Concentrated serum cholinesterase has shortened the period of paralysis (17), but has yet to be used in a case showing real sensitivity to succinylcholine.

Some authors have administered neostigmine (in pure desperation, I think), but since this is an anticholinesterase, it is not surprising that it was unsuccessful.

Large doses of nikethamide (up to 20 cc.) have apparently been successful (8), but in these instances it may well have been the induction barbiturate that caused the apnoea. My distinct impression in both cases 1 and 2 was that nikethamide did more harm than good, and in case 1 it certainly abolished the tiny respiratory movements that were present.

The following suggestions may prove helpful when a patient responds to succinylcholine with a prolonged apnoea.

1. Endeavour to control respiration without either hypo- or hyperventilation.
2. If an intravenous barbiturate has been given shortly before, administer picrotoxin.
3. Introduce a sudden strong concentration of ether vapour into the circuit. If

this results in coughing or straining then the apnoea is not due to peripheral paralysis.

4. If the patient has had both a long-acting relaxant as well as succinylcholine, neostigmine should not be given. Should the prolonged action be due to succinylcholine it will be very greatly extended, and if the longer acting relaxant is to blame recovery can be expected within an hour, without neostigmine.

5. Nikethamide is of doubtful benefit in these cases and unless strong suspicions are entertained that the intravenous barbiturate or other central respiratory depressants are causing the condition, it is better that the drug be witheld.

Except for concentrated serum cholinesterase, there appears to be no other remedy in these cases, and as a low serum cholinesterase is not an invariable finding, it is doubtful if even this would be of help in true sensitivity to succinylcholine.

Summary

Case histories of three patients have been given in an effort to show that a low serum cholinesterase is by no means an invariable finding where prolonged recovery to succinylcholine occurs.

A theory is given of a possible mechanism in these cases.

Practical suggestions on treatment are offered.

Résumé

L'auteur présente le cas de deux patients qui, sous l'effet de la succinyl choline, ne se reveillèrent qu'après deux heures et demie. Chez l'un, la cholinesterase du serum était normale; chez l'autre, elle était basse.

Par ailleurs, un troisième patient, chez qui la cholinesterase était basse avant l'opération, ne montra aucune réponse anormale à la succinyl choline.

On préconise la théorie d'un effet central dépresseur surajouté aux effets périphériques pour expliquer ces cas d'apnée prolongée due à la succinyl choline.

REFERENCES

1. Bovet, D., Bovet-Nitti, F., Guarino, S., Longo, V. G., and Marotta, M. R.C. 1st. Sup. Sanita *12*: 106 (1949). Quoted in Biology Abst. *24*: 32763 (1950).
2. Bovet-Nitti, F. 1st. Sup. Sanita *12*: 138 (1949). Quoted in Biology Abstr. *24*: 32764 (1950).
3. Evans, F. T., Gray, P. W. S., Lehmann, H. and Silk, E. Sensitivity to Succinylcholine in relation to Serum Cholinesterase. Lancet *1*: 1229 (1952).
4. Foldes, F. F., Vanderwort, R. S., Shanor, S. P. The Fate of Succinylcholine in Man. Anaesthesiology *16*: 11 (1955).
5. Cowan, C. A. Nine Hours Apnoea following Succinylcholine. Anaesthesia *9*: 23 (1952).
6. Harrison, B. L., Seward, E. H. and Skinner, L. C. Prolonged Scoline Apnoea Treated by Blood Transfusion. Anaesthesia *7*: 152 (1952).
7. Calvert, S., Lehmann, H., Silk, E. and Slack, W. R. Prolonged Apnoea after Suxamethonium. Lancet *2*: 354 (1954).
8. Barron, D. W. Scoline Apnoea. Brit. Med. J. *2*: 833 (1952).
9. Love, S. H. S. Prolonged Apnoea following Scoline. Anaesthesia *7*: 113 (1952).
10. Kennedy, H. J. Prolonged Respiratory Paralysis after Succinylcholine. Brit. Med. J. *1*: 866 (1952).

11. HEWER, L. C. Prolonged Respiratory Paralysis after Succinylcholine. Brit. Med. J. *1*: 971 (1952).
12. THESLEFF, S. and VON DARDELO, O. Nord Med. *46*: 1045 (1951).
13. LEHMANN, H. Succinylcholine. Lancet *2*: 199 (1952).
14. RICHARDS, H. and YOUNGMAN, H. R. The Ultra-Short-Acting Relaxants. Brit. Med. J. *1*: 1334 (1952).
15. FOLDES, F. F. Prolonged Respiratory Paralysis after Succinylcholine. Brit. Med. J. *1*: 1352 (1952).
16. BOURNE, J. G., COLLIER, H. O. J. and SOMERS, G. F. Succinylcholine (Succinoylcholine) Muscle-Relaxant of Short Action. Lancet *1*: 1225 (1952).
17. EVANS, F. T., GRAY, P. W. S., LEHMANN, H. and SILK, E. Effect of Pseudo-Cholinesterase Level on action of Succinylcholine. Brit. Med. J. *1*: 136 (1953).

METHYL N-PROPYL ETHER: A REPORT OF A CLINICAL TRIAL

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METHYL N-PROPYL ETHER was first described by Chancel in 1869, but its valuable anaesthetic properties were not appreciated until its inclusion in the long series of ethers tested by Krantz and his co-workers in the United States.

The clinical trials of methyl n-propyl ether following Krantz's original description of its anaesthetic properties and pharmacology in 1946 (1) showed that it might be superior to diethyl ether as an inhalation anaesthetic, in having the useful properties of diethyl ether in enhanced degree without some of its undesirable features.

Many further reports have stressed the advantages of methyl n-propyl ether over diethyl ether, and yet the agent has not gained any wide acceptance in clinical anaesthesia. It was in an attempt to determine the reasons for this lack of acceptance of this agent that the following study of methyl n-propyl ether was carried out.

CHEMISTRY AND PHARMACOLOGY

Methyl n-propyl ether is a colourless, highly inflammable, volatile liquid, with a characteristic ethereal odour. The physical and chemical properties of methyl n-propyl ether are in many ways similar to those of diethyl ether, as the two are isomeric. They may be summarized and compared as follows:

	Methyl n-propyl ether	*Diethyl ether*	*Ref.*
Formula	CH3-O-C3H7	C2H5-O-C2H5	
Description	volatile clear colourless liquids with characteristic odours		
S.G. at 15° C.	0.731	0.720	
B.P. at 760 mm. Hg.	39° C.	34.5° C.	
Vapour press. at 28° C.	520 mm. Hg.	597 mm. Hg.	(3)
Solubility in water (per 100 cc. at 25° C.)	5.0 ml.	8.6 ml.	
Oil/water coefficient	10 plus or minus 1	4 plus or minus 0.4	(2, 3)

Krantz and his co-workers (1, 3, 5) subjected this substance to extensive experiments on rats, dogs, and Macacus Rhesus monkeys. Their findings may be summarized as follows:

1. Methyl n-propyl ether produced no significant histological change in the livers of animals and did not interfere with hepatic function as demonstrated in the bromsulphalein test (1).

2. It produced no pathological changes in the kidney nor alterations in the urine (3).

3. It produced no significant changes in CO_2 combining power, urea nitrogen, or clotting time of the blood (1).

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4. It caused no abnormalities in ECG tracings, pulse, or blood pressure (1, 6).

5. In the dog, it is approximately 25 per cent more potent than diethyl ether. Its anaesthetic index (ml/kg required for respiratory arrest)/(ml/kg required for surgical anaesthesia) was 2.5, compared to 2.1 for diethyl ether, and 1.6 for chloroform (1, 6).

6. Prolonged anaesthesia in dog and monkey did not give rise to detectable methyl alcohol or formaldehyde in the blood, indicating that, like diethyl ether, methyl n-propyl ether is not metabolized in the body (3).

Previous Clinical Trials

In their series of cases White *et al.* (6) found that, compared with diethyl ether, methyl n-propyl ether was less irritating to the respiratory tract, induction with it smoother, the pulse rate not as rapid, and muscular relaxation more easily achieved. Post-operative nausea and vomiting were less, and there were no pulmonary complications. They state that it might be used alone as an induction agent, and Rochberg (8) and Rees (12) state that if other induction agents are used, the change to methyl n-propyl ether is made more smoothly and easily than with diethyl ether. All writers agree that respiration under methyl n-propyl ether anaesthesia is quiet, unhurried, and moderately deep (6, 9, 12).

Although complaints are on record (7) by operating teams against its odour, it stands high on a list of anaesthetic agents arranged in order of decreasing pleasantness of odour (3).

Fisher and Whitacre (7) in 1947 concluded, in a series of over five hundred cases, that decreased irritation of the respiratory tract was the agent's only advantage over diethyl ether.

Shane (9) claimed that anaesthesia with methyl n-propyl ether gave better relaxation of the abdominal musculature and contraction of the intestines than that obtained with diethyl ether.

Redgate and Bannister (11) report a case in which overdose of the drug resulted in depression of the cardiovascular system, but Shane (9) states that in ordinary concentration it has no effect on cardiovascular function. Barnett (16) reported two cases of cardiovascular depression, but states they responded rapidly to lightening of the methyl n-propyl ether anaesthesia. Rochberg (8) reported the tendency to capillary oozing to be reduced.

Sykes (10) found the chief points of interest to be the lack of irritation of the respiratory tract and the small number of pulmonary and gastric complications.

Rochberg (8), Dawkins (13), and Kaplan (14) all reported a very short recovery period, which was generally pleasant. However Middleton and Picken (15) reported no significant alteration in the incidence of postoperative nausea and vomiting as compared with that found when using diethyl ether.

Clinical Trial

With these proposed advantages and disadvantages in mind the agent was used in a carefully documented series of over 150 cases.

Patients were unselected as regards age (which varied from sixteen months to seventy-seven years), operation proposed (which included all types of major and

minor surgery, including thoracic, cardiac and intracranial cases), or physical condition. Duration of anaesthesia varied from fifteen minutes to five hours and forty minutes.

The agent was used in all available methods and techniques, which included open and semi-drop, fractional rebreathing, non-rebreathing, semi-closed and closed circle absorber systems.

Preoperative medication was that routinely employed for other methods of general anaesthesia, and consisted of an opiate and a belladonna drug one hour before operation. In the case of children, atropine and rectal Pentothal® were used in most cases.

Induction

Induction was consistently smooth. The lack of irritation of the respiratory tract as demonstrated by the persistent absence of coughing, breath-holding, and spasm was a very marked feature of the agent.

Induction was generally rapid, except in those cases where methyl n-propyl ether alone was used by the open drop method. It does not vaporize as readily as diethyl ether, and as a result is slower in action; some other agent was therefore generally used in conjunction.

Maintenance

Methyl n-propyl ether was used with a wide variety of agents including divinyl ether, trichlorethylene, cyclopropane, nitrous oxide, and Pentothal®, as well as various muscle relaxants. The change from another agent to methyl n-propyl ether was found to be routinely smooth and much more rapidly accomplished than the change to diethyl ether might be expected to be.

Maintenance was consistently uneventful. Because of the low volatility of the agent it was found most effective in closed circle systems. A slow pulse was usually present; a fall in blood pressure was noted only with very deep anaesthesia, and this was never severe. Cardiac irregularities did not occur. The marked cardiovascular depression reported was not encountered.

Respiration was quiet and generally slow in contrast to the respiration noted with diethyl ether. Patients could be carried in light planes of anaesthesia without bucking or breath-holding.

The degree of muscle relaxation of both jaw and abdominal wall was felt to be markedly better than that obtained with comparable levels using diethyl ether. Intubations were accomplished with ease routinely under excellent relaxation. Quietness and constriction of the bowel were frequently commented upon; in some cases the surgeons compared the abdomen to that obtained only with spinal analgesia. In obstetrical cases the degree of relaxation was always satisfactory for intrauterine manipulations.

One technical complication arose owing to the fact that the patient's eyeball tends to rove at all levels of anaesthesia; therefore the agent was soon rejected for ophthalmological cases.

Recovery

The recovery time from methyl n-propyl ether anaesthesia was considered to be shorter than that which might be expected in comparable cases using diethyl

ether. Postoperative nausea and vomiting were never severe, and the incidence was about 15 per cent. Immediate or remote postoperative complications attributable to the agent did not occur in this series.

Unpleasant Odour

The references to the unpleasant odour of the agent were confirmed. Despite the fact that the patient breathes the agent without evidence of irritation, and recovers from its use without undue nausea and vomiting, the unpleasant odour soon led to its use being restricted to the closed circle system to prevent complaints of headache and other uncomplimentary comments from operating-room personnel.

Summary

This is a brief report on the use of methyl n-propyl ether in over one hundred and fifty unselected cases undergoing all types of surgery. The agent was used by all available techniques and methods.

Smooth induction or changeover from other agents was noted, with extremely little irritation of the respiratory tract. Maintenance was not difficult and was characterized by quiet respiration, a slow pulse, and consistently excellent muscle relaxation. Cardiovascular depression was not a problem in this series.

The main disadvantage of the agent is its disagreeable odour.

Methyl n-propyl ether appears to have some specific advantages over diethyl ether, and thus deserves a definite but limited place in the practice of anaesthesia.

Résumé

L'auteur expose brièvement les constatations qu'il a fait en utilisant l'éther méthyle N-propyle dans plus de cent cinquante cas non choisis qui subirent différentes interventions chirurgicales. L'agent anesthésique fut employé avec toutes les techniques et méthodes disponibles.

Il fut noté que l'induction ou bien l'emploie après d'autres agents se faisaient sans difficulté et sans notable irritation du système respiratoire. L'anesthésie fut maintenue aisément et se caractérisa par une respiration facile, un pouls lent et un excellent et constant relâchement musculaire. La dépression cardiovasculaire ne fut pas un problème dans cette série.

Le désavantage principal de cet agent est son odeur désagréable.

L'éther méthyle N-propyle semble avoir des avantages spécifiques sur l'éther diéthyle et c'est pourquoi il a une place définie mais limitée dans la pratique anesthétique.

REFERENCES

1. Krantz, J. C. Jr., Evans, W. E. Jr., Carr, J. C. and Kibler, D. V. J. Pharmacol. & Exper. Therap. *86*: 138 (1946).
2. Carr, C. J., Kibler, D. V. and Krantz, J. C. Jr. Anesthesiology *5*: 495 (1944).
3. ——— Anesthesiology *8*: 53 (1947).
4. Kibler, D. V. Anesthesiology *8*: 288 (1947).
5. Krantz, J. C. Jr., Carr, C. J., Iwamoto, H. K. and Sauerwald, M. J. Anesthesiology *8*: 497 (1947).

6. WHITE, M. L. T., SHANE, S. M. and KRANTZ, J. C. Jr. Anesthesiology 7: 663 (1946).
7. FISHER, A. J., WHITACRE, R. J. Anesthesiology 8: 156 (1947).
8. ROCHBERG, S. Anesthesiology 8: 637 (1947).
9. SHANE, S. M. Anesth. & Analg. 26: 260 (1947).
10. SYKES, C. E. Brit. Med. J.: 420 (1949).
11. REDGATE, J. W. and BANNISTER, A. K. Anaesthesia 5: 183 (1950).
12. REES, G. J. and GRAY, T. C. Brit. J. Anaesth. 22: 83 (1950).
13. DAWKINS, C. J. M. Anaesthesia 5: 81 (1950).
14. KAPLAN, B. Anaesthesia 6: 231 (1951).
15. MIDDLETON, H. G. and PICKEN, D. K. W. Brit. Med. J.: 1192 (1954).
16. BARNETT, M. S. Anaesthesia 9: 153 (1954).

THE ROLE OF CARBON DIOXIDE IN ANAESTHESIA*

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DUNCUM in her book "The Development of Inhalation Anaesthesia" (1) states that carbon dioxide was the first gaseous anaesthetic used surgically and mentions that Hickman performed surgical operations on animals under the influence of carbon dioxide as early as 1824. Recently, a large meat-packing organization introduced the novel procedure of using 30 per cent carbon dioxide as an inhalational anaesthetic for hogs, thereby reducing the noise, confusion, labour, and time required in slaughtering operations (2).

Be that as it may, carbon dioxide today plays a very important role in modern anaesthesia. I would like to spend a few moments reviewing with you some of the physiology of carbon dioxide. CO_2 is the most important end-product of tissue metabolism. As such, CO_2 is constantly being produced by the cells, and is carried by the blood to the lungs for excretion. In the blood, CO_2 exists in three forms: (1) as free carbon dioxide, which is dissolved in the water of the blood, (2) as bicarbonate of the plasma, and (3) as carbamino compounds in combination with haemoglobin. The amount of free dissolved carbon dioxide determines the tension or partial pressure of the gas. It is the difference in partial pressure of CO_2 which is responsible for CO_2 transport.

For example, the CO_2 tension of the body cell is greater than that in the capillary blood, thus CO_2 moves into the blood. Similarly, the partial pressure of CO_2 in mixed venous blood, $P\bar{v}CO_2$ (3) (normally 46 mm. Hg.) is greater than that in the alveoli of the lungs, $PACO_2$ (normally 40 mm. Hg.). Thus CO_2 leaves the blood, enters the alveoli, and is subsequently exhaled. The $PACO_2$ is therefore maintained at a constant level and this value is the same as in the arterial blood. The partial pressure or tension of CO_2 in the arterial blood is referred to as the $PaCO_2$.

It is well known that the pH of the blood is maintained at 7.40 despite the constant production of acid metabolites. This is because of the presence of various buffers in the blood, of which the bicarbonate buffer is the most important, both because of its high concentration and because of its ease of alteration. The body pH is maintained at 7.40, then, because of the constancy of the buffer ratio bicarbonate/carbonic acid which is normally 20/1. In the laboratory, one can use the Henderson-Hasselbalch Equation (4) to calculate $PaCO_2$:

$$pH = 6.1 + \log \frac{(H\,CO_3'p)}{0.0301\,PaCO_2}.$$

As may be seen, a decrease in this ratio will lead to a decrease in pH. This acidosis may be due either to a decrease in the plasma bicarbonate ion concentration or, on the other hand, to an increase in the $PaCO_2$.

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If the major change is a decrease in plasma bicarbonate ion concentration, as, for example, in diabetic acidosis, the buffer ratio and, thus the pH, will decrease. This is referred to as *metabolic acidosis.*

When the $PaCO_2$ increases, with the bicarbonate ion concentration remaining about the same, the ratio decreases and so does the pH. This is referred to as *respiratory acidosis.*

In health, therefore, the maintenance of a constant pH depends upon our keeping the $PaCO_2$ at a normal level, which in turn depends upon the adequate elimination of CO_2 by the lungs. This now brings us to a consideration of ventilation.

The tidal volume, or the volume of gas moved in and out of the lungs with each breath, can be divided into two parts. Some of the gas never reaches the alveoli, but remains in the bronchi, trachea, and oropharynx. This gas occupies the dead space volume, so named because as far as respiration is concerned, it is dead or useless—it does not undergo gas exchange. The other and important part of the tidal volume is that portion which does reach the alveoli of the lungs and which undergoes gas exchange, that is, the removal of CO_2 and the uptake of oxygen.

The control of respiration is both chemical and nervous. The chemical control is the $PaCO_2$, which acts directly on the respiratory centre in the medulla. If the $PaCO_2$ of a normal patient rises, the respiratory centre is stimulated. This results in an increase in ventilation and greater CO_2 elimination. The $PaCO_2$ is thus returned to its normal value of 40 mm. Hg. Hypoxaemia, or a low partial pressure of oxygen (PaO_2), is also a stimulus for increased ventilation, but it brings about its effect by a different route—by acting on the chemoreceptors of the carotid and aortic bodies and then reflexly influencing the respiratory centre. However, in cases of asphyxia, in which the PaO_2 is decreased and the $PaCO_2$ is increased, the hypoxaemic stimulus plays an insignificant role in the resultant increased ventilation. It is the elevated $PaCO_2$ which stimulates ventilation. A $PaCO_2$ rise of 5 mm. Hg. will result in increased ventilation. However, the PaO_2 would have to decrease by about 60 mm. Hg. from a normal value of 100 mm. Hg. to about 40 mm. Hg. before hypoxaemia would stimulate ventilation. This would correspond to breathing 12 per cent instead of 21 per cent oxygen, or breathing air at an altitude of 13,000 feet.

Thus, we breathe primarily to get rid of carbon dioxide. We must maintain an adequate alveolar ventilation to keep our $PaCO_2$ and pH at normal levels. A decreased alveolar ventilation, from whatever cause, will result in an elevated $PaCO_2$—hypercapnia, and a decrease in pH—respiratory acidosis.

From the respiratory point of view, the aim of the anaesthetist should be to maintain normal respiration. This implies normal gas exchange, both for oxygen and carbon dioxide, and can only be accomplished by adequate alveolar ventilation.

Let us now consider the state of the respiratory gases in the alveoli of the lungs a few minutes after a patient has been breathing a high concentration of oxygen. The nitrogen in the lungs will be washed out and the alveolar oxygen tension (P_AO_2) will rise from 100 mm. Hg. to about 600 mm. Hg. On the basis of a

functional residual volume of 2500 cc., some 1800 cc. of oxygen could be absorbed before the P_AO_2 would fall to its previous level of 100 mm. Hg.—if no additional ventilation took place. Thus the oxygen needs in such a patient could be supplied for at least ten minutes or longer—in the absence of any additional ventilation.

However, within a few seconds the alveolar CO_2 tension would become equal to that of the mixed venous blood and accumulation of the CO_2 would begin in the blood and tissues. This example stresses the importance of an adequate alveolar ventilation.

Let us now consider a patient who has a dead space of 150 cc., tidal volume of 600 cc., and a respiratory frequency of 14/minute. His alveolar ventilation per breath is 600—150 or 450 cc. and his alveolar ventilation per minute is 450×14, or 6300 cc. An anaesthetic mask is now applied which has a dead space of 150 cc. His minute alveolar ventilation will be $(600—150—150) \times 14$, or 4200 cc., if frequency and tidal volume remain the same. Therefore, with the same minute volume of expired air ($600 \times 14 = 8400$ cc.) the addition of the anaesthetic mask has reduced his alveolar ventilation by 30 per cent.

The tidal volume usually increases to compensate for this added dead space in an attempt to maintain a constant alveolar ventilation. In this patient the tidal volume would have to be 750 cc. (an increase of 25 per cent) to maintain the same alveolar ventilation, if respiratory frequency were unchanged.

Anaesthetic agents are known depressants of central nervous system function. The respiratory centre is also depressed, and this is important for two reasons. In the first place, these agents will decrease ventilation with a resultant rise in $PaCO_2$ and respiratory acidosis. Secondly, the sensitivity of the respiratory centre will be lowered, so that the elevated $PaCO_2$ loses its effectiveness as a stimulus to increase the ventilation.

It has been well documented that a small decrease in minute ventilation volume occurs in modern anaesthesia, and the resultant decrease in alveolar ventilation will cause the $PaCO_2$ of the blood, and thus of the body cells, to become elevated when respiration is unassisted. The $PaCO_2$ may rise to narcotic levels and values of 100 mm. Hg. and over have been recorded.

Buckley (5) studied 31 non-thoracic cases during cyclopropane anaesthesia. In 15 cases in which respiration was unassisted, the average $PaCO_2$ at the end of anaesthesia was 85 mm. Hg. (equivalent to 12.3 per cent CO_2), more than twice the normal value and with a range of 55 to 150 mm. Hg. (8–20 per cent). In 16 cases in which respiration was assisted, the rise in $PaCO_2$ was much less, the average highest $PaCO_2$ being 47 mm. Hg. (6.8 per cent).

In one series of pneumonectomies (6) with the patient in the lateral position and performed with respiration unassisted, the $PaCO_2$ rose from 35 to 98 mm. Hg. When a similar operation was done in the prone position, using an Overholt table, the $PaCO_2$ rose to only 47 mm. Hg. Other investigators have shown the value of assisted, controlled, or artificial respiration and have been able to keep the $PaCO_2$ from rising during a pneumonectomy.

Inadequate alveolar ventilation during anaesthesia may be due to several factors. Impaired function of the respiratory centre by preoperative and anaesthetic drugs and the effect of position have been mentioned. Other factors which

must be considered are: the use of relaxants, the presence or absence of pulmonary collapse, obesity, operations on the open chest, the Trendelenburg and prone positions, and the use of kidney or gall bladder rests. Most of these factors are important in thoracic operations, while others play an important role in non-thoracic cases.

What are the deleterious effects of hypercapnia during anaesthesia? If the $PaCO_2$ is allowed to rise during anaesthesia, there may be a considerable delay in the patient's return to consciousness. Similarly, it may take a few hours before the respiratory acidosis is relieved, and the $PaCO_2$ returns to normal. Brown and co-workers (7) at Minnesota described severe electrocardiographic changes in dogs after release from high CO_2 tensions. Eleven of these fifteen animals developed ventricular fibrillation.

Assisted respirations, therefore, are frequently necessary during anaesthesia to maintain an adequate alveolar ventilation so that the $PaCO_2$ does not rise and so that respiratory acidosis does not occur.

This reminds me of a quotation I heard a Professor of Anaesthesia once make. He said, "Look on acidosis like sin; be against it."

I would now like to say a few words about the syndrome of CO_2 narcosis, a condition which we are recognizing more and more in the patient with severe respiratory insufficiency. Ventilation tracings of a normal individual and of a patient with chronic pulmonary emphysema are shown in Figures 1 and 2.

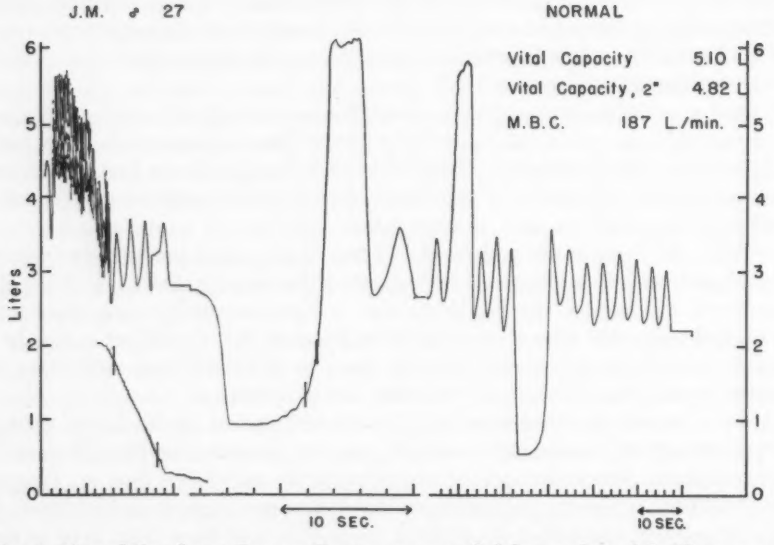

FIG. 1—*Normal Ventilation Tracing.* Tracing was recorded from right to left. The two marks on the vital capacity curve represent the one-second and two-second vital capacities which constitute 82 per cent and 95 per cent of the total. The maximum breathing capacity (M.B.C.) is shown at the extreme left. The lower pen, which is geared to the upper pen in a 25:1 ratio, measures the total volume of air moved during the test.

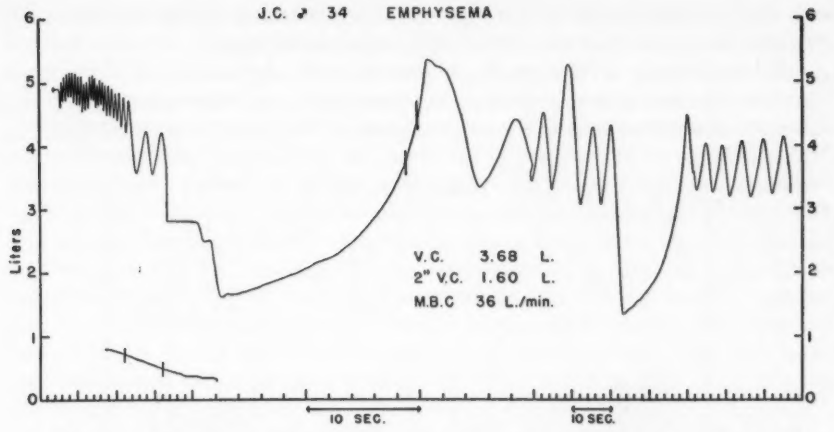

FIG. 2—*Tracing from a case of chronic pulmonary emphysema.* The one-second and two-second vital capacities are 24 per cent and 44 per cent of the total. Compare with Figure 1. The decreased total and one-second vital capacity, and the reduced M.B.C., indicate severe obstructive ventilatory insufficiency.

Patients with chronic pulmonary emphysema, for example, have great difficulty ventilating their lungs. As a result, alveolar ventilation becomes inadequate, the $PaCO_2$ rises and the PaO_2 decreases. The high $PaCO_2$ results in respiratory acidosis, and the low PaO_2 produces arterial oxygen unsaturation and cyanosis. The elevated $PaCO_2$ should act as a respiratory stimulant, but these patients are unable to increase their ventilation because of their increased pulmonary resistance. Finally the respiratory centre becomes completely insensitive to the $PaCO_2$ stimulus. What then controls the ventilation and respiration of these patients? They are now breathing only in response to their oxygen lack. A patient in such a precarious respiratory state may be admitted to the medical ward, possibly with a patch of pneumonia which has taken away a further portion of his functioning lung tissue. The unwary interne, who on examination finds a markedly dyspnoeic, deeply cyanosed patient with râles at both bases, may order morphine for the supposed pulmonary oedema, and oxygen for correction of the cyanosis. He is unfortunately "killing him with kindness" for he is making two mistakes. The morphine will depress the respiration rate, and thus further reduce alveolar ventilation. But more important, he has taken away this man's only stimulus to breathing. The oxygen therapy corrects the hypoxaemia, and alveolar ventilation is further reduced. The $PaCO_2$ soon rises to narcotic levels and the acidosis may cause respiratory arrest and death.

This is the syndrome of CO_2 narcosis. The anaesthetist must be cognizant of the problems of these patients, for he may have to administer an anaesthetic or help in their resuscitation. We have seen that alveolar underventilation and the associated rise in $PaCO_2$ occurs during anaesthesia in patients with normal cardiopulmonary function. The dangers, then, of CO_2 retention and respiratory acidosis are even greater in a patient who has pulmonary disease. The patient

with chest disease may have been given a narcotic before operation, and during operation the gas mixture may have a high tension of oxygen.

Another example is the group of patients with kyphoscoliosis. The major ventilatory defect in these patients is the greatly reduced vital capacity. Figure 3 shows the ventilation tracing from such a patient. Preoperative physical examina-

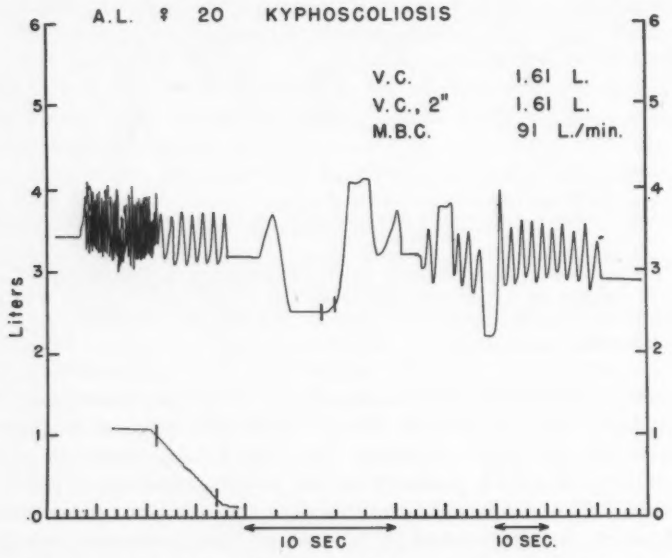

FIG. 3—*Tracing from a case of kyphoscoliosis.* This is an example of restrictive ventilatory insufficiency. The per cent one-second vital capacity and the M.B.C. are normal, but the total vital capacity itself is greatly reduced.

tion may otherwise be normal and they may not complain of any dyspnoea. Since their tidal volume is limited because of the reduced vital capacity, they depend upon an adequate respiratory frequency to maintain alveolar ventilation. If the respiratory rate of a normal individual is reduced, the tidal volume will increase in a compensatory manner. However, these patients with kyphoscoliosis are unable to increase their tidal volume because of their limited chest expansion. Thus, after preoperative morphine, respiratory rate is slowed, tidal volume is fixed, and alveolar underventilation occurs. As a result, $PaCO_2$ rises and again we have the complications of respiratory acidosis, CO_2 narcosis, and possibly death. This may occur on the ward either before or after operation. The same situation may also occur in patients with Marie-Strümpell's arthritis, or in the other types of arthritis in which there is costal fixation and restricted chest expansion.

CO_2 also produces vascular effects. An increased $PaCO_2$ results in a stimulation of the chemoreceptors, which act on the vasomotor centre to produce peripheral vasoconstriction. An elevated $PaCO_2$ also acts locally, producing vasodilation.

The resultant effect of hypercapnia on the level of blood pressure will be a balance between these two actions. Usually, the central effect predominates. Buckley (5), for example, showed that the hypertension encountered during cyclopropane anaesthesia was related to the duration of hypercapnia.

The syndrome of so-called "cyclopropane shock" is well known to anaesthetists. Some experimental observations are pertinent in this respect. In 1927, Goldstein and Dubois (8) showed in normal individuals that during a re-breathing experiment in which the CO_2 elimination was decreased, the blood pressure rose. They also showed that following the cessation of re-breathing, there was a marked fall in blood pressure. In those cases which develop cyclopropane shock, the $PaCO_2$ is markedly elevated at the time the anaesthetic is discontinued. The precipitating factor in producing this syndrome seems to be that as the anaesthesia wears off, excess CO_2 is blown off at a more rapid rate with the result that the buffer mechanisms can no longer cope with the situation, and rapid pH changes occur. This syndrome is seen more frequently when cyclopropane is used, because of the marked respiratory centre depression which cyclopropane produces. However, it may be seen with other types of anaesthesia that are associated with marked hypercapnia and respiratory acidosis.

Finally, I would like to say a word about the use of 5 per cent carbon dioxide in oxygen (carbogen) as a resuscitating agent. Individuals who are in need of resuscitation are already in a state of respiratory insufficiency. They are already in a state of hypercapnia and respiratory acidosis. The aim of resuscitation, then, is the improvement of alveolar ventilation to ensure an adequate oxygen tension, and also to remove the excess body CO_2. As we have seen, with high tensions of CO_2 the sensitivity of the respiratory centre is lowered so that it can no longer respond to this endogenous CO_2 stimulus. How then can exogenous CO_2 (as 5 per cent CO_2 in oxygen) be expected to stimulate respiration? It can only lead to more severe respiratory acidosis. The simultaneous administration and vigorous removal of a therapeutic agent is treatment reduced to absurdity.

In closing, I would like to repeat the admonition: "Look on acidosis like sin; be against it."

Summary

The physiology of CO_2 is briefly reviewed. Inadequate alveolar ventilation does occur during anaesthesia in normal individuals, and this results in CO_2 retention and respiratory acidosis. Some of the contributing factors to this undesirable result are discussed; they include the use of preoperative and anaesthetic drugs, and the position of the patient. The syndrome of CO_2 narcosis is discussed. The vascular effects of hypercapnia are reviewed in relation to the syndrome of cyclopropane shock. Five per cent CO_2 in oxygen is not recommended as a resuscitating agent.

Résumé

Le dioxyde de carbone, dissous dans l'eau du sang artériel, détermine la pression partielle du CO_2. Celle-ci est appelée $PaCO_2$. Le rapport de la concentration de l'ion bicarbonate du plasma sur le $PaCO_2$ détermine le pH du sang artériel. Le

contrôle chimique de la respiration étant le $PaCO_2$, on comprend que le volume minime de ventilation alvéolaire (cette partie de la ventilation totale qui subit un échange gazeux), le $PaCO_2$ et le pH du sang artériel, sont intimement liés l'un à l'autre. Si un patient respirant un mélange gazeux riche en oxygène arrêtait de respirer, ses besoins organiques en oxygène seraient satisfaits pour 10 minutes. Cependant, en quelques secondes, cette diminution de la ventilation alvéolaire résulterait en une élévation du $PaCO_2$ et en une acidose respiratoire. Une telle diminution de la ventilation alvéolaire peut se présenter en anesthésie moderne chez des patients à fonction cardio-pulmonaire normale. La position du patient et l'effet des agents préopératoires et anesthésiques sur le centre respiratoire sont parmi les plus importants facteurs susceptibles d'affecter la ventilation durant l'anesthésie.

Le syndrome de narcose au CO_2 se rencontre fréquemment chez les patients souffrant de maladie pulmonaire chronique ou encore qui ont une scoliocyphose. L'anesthésiste doit être au courant des problèmes qui comportent ces patients car il peut être appelé à les anesthésier ou encore à faciliter leur ressuscitation.

Le CO_2 produit aussi des effets vasculaires. Buckley a démontré que l'hypertension produite lors d'une anesthésie au cyclopropane était attribuable à la durée de la retention du CO_2. De même, dans les cas qui développent un choc au cyclopropane, le $PaCO_2$ était très élevé quand cet agent fut discontinué.

L'usage de dioxyde de carbone à 5 pour cent dans l'oxygène comme agent ressuscitateur ne doit pas être recommandé parce que les patients qui ont besoin de ressuscitation sont déjà dans un état d'insuffisance respiratoire et un tel traitement peut seulement conduire à une acidose respiratoire plus sévère.

REFERENCES

1. Duncum, B. M. The Development of Inhalation Anaesthesia. London: Oxford University Press (1947).
2. Drill, V. A. Pharmacology in Medicine. New York: McGraw-Hill (1954). Page 55/14.
3. Standardization of Definitions and Symbols in Respiratory Physiology. Federation Proc. *9*: 602–5 (1950).
4. Davenport, H. W. The ABC of Acid-base Chemistry. 3rd ed., Chicago: University of Chicago Press (1950).
5. Buckley, J. J., Van Bergen, F. H., Dobkin, A. B., Brown, E. B., Miller, F. A. and Varco, R. L. Postanesthetic Hypotension following Cyclopropane: Its Relationship to Hypercapnia. Anesthesiology *14*: 226–37 (1953).
6. Personal communication.
7. Brown, E. B. and Miller, F. Ventricular Fibrillation following a Rapid Fall in Alveolar Carbon Dioxide Concentration. Am. J. Physiol. *169*: 56–60 (1952).
8. Goldstein, J. D. and DuBois, E. L. The Effect on the Circulation in Man of Rebreathing Different Concentrations of Carbon Dioxide. Am. J. Physiol. *81*: 650–60 (1927).

THE PRACTICE OF MEDICINE IN ANCIENT ROME*

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IN ancient Rome, as in all primitive societies, the practice of medicine began as a mixture of magic and religion, and remained almost entirely so until the time of Cato. Tacitus speaks of Rome as "a city where superstition interpreted everything," and said that Vespasian cured a blind man with his spittle, and a paralysed limb by treading on it. Western medicine even today has some religious and magical elements; religious restrictions still exert their influence in modern practice, and we use such new names as "psychosomatic," "complexes," and "conditioned reflexes," to describe ideas that the ancients ascribed to magic.

The idea of magician-priest-physician was a logical concept. If the magician-priest can foretell events and placate the gods, he should be able to diagnose disease, prognosticate its course, and bring divine intervention for its cure. This, of course, has to do with internal diseases, but wounds and injuries occur in all communities, and for the treatment of these, empirical methods are usually quickly evolved. In early medicine, therefore, surgery tends to be more efficient than medical therapy.

Our knowledge of Etruscan medicine is vague and uncertain. Divination played an important part, and it was based upon the examination of the viscera of animals, especially the liver. The augurs were members of a religious college whose function was to interpret signs of approval or disapproval of the gods in reference to any proposed undertaking. There were many methods, but an important one was the examination of the entrails of sacrificial animals. Anything abnormal was brought to the attention of the augurs, but its interpretation was usually left to the Etruscan Haruspices. Castiglioni suggests that the Latin word "haruspex" possibly comes from the Chaldean "har" meaning liver.

Although divination was employed for the interpretation of the will of the gods and for prognosis in disease, more rational methods of treatment were also known. The beneficial effects of the thermal waters of ancient Etruria had been known from very early times. Castiglioni states that there is some evidence that the Etruscans knew of the relationship of marshy lands to certain fevers. They had some dental knowledge, for dental work by means of gold wire has been found among Etruscan remains. Theophrastus quotes Aeschylus as saying that Etruria is rich in medicine, and that the Etruscan race is one that cultivates the practice of medicine.

From early days the Romans had some measures of public hygiene. There was strict supervision of prostitution. Burial of the dead within the city walls was forbidden by the law of the twelve tables. There was an adequate water supply in Rome from early times, and this was gradually extended. It has been estimated

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that in the time of the Empire more than one hundred gallons per person daily were available, in addition to that used in the public baths. This is greater than the available supply of large modern cities, but Carcopino has pointed out that in very few instances was any of this supply available in the houses of the ordinary citizen. Although the Roman sewage system took care of the public latrines it did not take care of those in private houses; the poorer householder had recourse to diverse methods of taking care of this need. Juvenal refers to the occasional unfortunate consequences for the passer-by. Even in the time of Trajan open malodorous trenches were still in existence. Up to the year 300 B.C. people drank the water of the Tiber, but at that time the aquaduct of the Aqua Appia was constructed supplying a purer drinking water. Fifty years later a second aquaduct was built, and subsequently others. The drainage of swamps adjacent to the city was necessary and this work was at first supervised by the censors. In the time of Augustus special magistrates were appointed for this duty.

In the time of the kings and of the early Republic medicine was still almost entirely based upon magic. The Romans had a host of lesser deities held to be responsible for physiological functions, disorders of which could be righted by appropriate offerings. Even at this early time the Romans were close to the Sicilian schools, and had some contact with Greek civilization, so that some glimmering of Greek medicine must have reached them. Although there were so-called physicians in Rome from the fourth century B.C. there were no truly professional practitioners until the arrival of Greek physicians. The first of these was probably Archagathus of the Peloponnesus who established himself at Rome in 219 B.C. He is said to have received Roman citizenship. At first he achieved great popularity and was given the name "Vulnerarius," but later his reputation suffered because of his cruelty in surgery, and he became known as "Carnifex."

Cato (B.C. 234–149) was the great opponent of the introduction of all things Greek, and especially of Greek medicine. He spoke of the Greeks as "a scoundrel and incorrigible race." He practised medicine in his own household, and thought that cabbage was a universal remedy. If this vegetable, either internally or externally, would not cure a sick slave he recommended that the slave be sold. Pliny has described the familiar remedies which Cato used for family, slaves, and domestic animals. He sought to cure dislocations by reciting gibberish; the actual words were, "huat, hanat ista pista sista domina damnaustro luxato"; this incantation was to accompany the sacrifice of a white sparrow. According to Pliny, Cato, in his dislike of the Greek physicians, even accused them of poisoning the sick. As a result of his influence difficulties were raised against the immigration of Greek physicians. In spite of this they continued to arrive in Rome, and the practical-minded Roman soon recognized their superior knowledge and education.

With the downfall of the Alexandrian Empire, Alexandria became the centre of medical education and progress, for the Hellenic influence still remained vigorous there after the decline of Hellenic freedom. The Alexandrian school was characterized by erudition, idealism, and technical dexterity. After the absorption of Egypt into the Roman Empire, Alexandria rapidly declined in importance. Its school had previously made many advances in medical knowledge, and for some

time it still remained a centre of medical education. It is almost certain that dissection was allowed and physiological experiments carried out. Alexandria became the means of preserving Greek texts, and of spreading Greek teaching to the east. According to Ovid and Livy, the cult of Aesculapius was introduced into Rome in the form of a huge serpent from Epidaurus, representing the god in his Chthonian aspect, in the year 293 B.C., but, as we have seen, it was at a later date that the Greek physicians began to arrive.

The most eminent of them came from Asia Minor, from the schools of Pergamus, Ephesus, and Miletus. Greek medicine was finally established in Rome as a profession through the personality, tact, and superior ability of Asclepiades of Bithynia. He was born in 124 B.C. and came to Rome about 100 B.C. He was well educated, of unusual intellect, and had a pleasant personality. He became a friend of many important Romans. He taught rhetoric, but found it unprofitable. When he began the practice of medicine he found that this knowledge helped him enormously. He was enough of a charlatan to make a popular practitioner. He knew his Romans, and his treatment was pleasant. There were no emetics, drastic purgatives, or bitter medicine; his most frequent prescription was wine, and he advised rest, massage, and a swinging couch. If his patients died they died in comfort. Lucius Apuleius tells of a case where Asclepiades restored to life a supposedly dead man who was being carried to the already lighted funeral pyre. His theory of medicine was based upon the atomic philosophy of Democritus and Epicurus; he ascribed disease to changes in the relation of atoms and pores, and rejected the humoral doctrines. He said that people might cease to consider him a doctor if he were ever taken ill himself. He was fortunate in this matter for, according to Pliny, his death was due to a fall from a ladder.

Along with the educated physicians, quacks and charlatans of all kinds flocked to Rome. There were many so-called specialists, and it is probable that many of these were so ignorant that they pretended to special knowledge of some branch of medicine, and so were not called upon to expose their ignorance by attempting to deal with all diseases. Many of these practitioners travelled from place to place, as a fertile field for their activities existed outside of Rome. One of the commonest specialties was ophthalmology, but most of these practitioners were principally concerned with producing new eye salves which they stamped with their names. Nearly two hundred seals for this purpose have been found, many exhibiting incorrect spelling. A few of the able practitioners, and more of the quacks, became very wealthy. It is said that Zenophon, a court physician, received the equivalent of twenty-five thousand dollars a year from the Emperor, and complained that he could have obtained more in private practice. Charmis, a hydrotherapist, or water doctor, as they were called, of Marseilles, was paid ten thousand dollars by one patient. At the other extreme the less popular physicians were sometimes compelled to take more lucrative callings to escape starvation. Martial refers to one who became an undertaker's assistant,

> "Dialus, who was once a surgeon,
> Now assists an undertaker;
> Here at length he finds the office
> To which alone his skill is suited."

With an excess of trained physicians, as well as of disreputable practitioners, many evils arose. Scientific effort was abandoned, and medicine was practised only for material gain. Wealthy patients were flattered. Professional jealousy led to unseemly criticism of fellow practitioners. Galen complains, "There is no distinction between robbers and physicians, except that the former commit their misdeeds in the mountains, the latter in Rome." The public loved to be swindled then, as it does today, and Pliny says, "People who understand no Greek place no confidence in the physician who does not practice in the Grecian style; indeed, they have less confidence when they understand what serves to cure them." The Greek doctors who had been well trained were sought out, and, as a result, other practitioners were gradually compelled to learn what they could of Greek medicine. There was a great demand for Greek texts. Pompey, for instance, brought some Greek medical literature to Rome, and his freedman, Lenaeus, translated it into Latin. Thus we see that professional medicine in Rome was henceforward Greek, and its most prominent representatives belonged to the Greek nation.

What then was the position of the physician in Rome? As we have seen, the first practitioners to come to the city were Greek adventurers, and not the best representatives of Greek medical science. Their social status was low, for which there were many reasons. There was the opposition of men like Cato, and the low type of many so-called physicians only increased the innate contempt of the Romans for professional medicine. The teaching of rhetoric and philosophy, and practice in the law courts were thought to be the only professions worthy of the Roman patrician. Anyone was free to practise medicine without scrutiny of his qualifications. There was a close relationship between the poorer type of practitioner and the drug-sellers who dealt in love potions, cosmetics, abortifacients, and poisons. By the time of the Empire, even famous physicians lent themselves, often under duress, to the preparation of poisons for the emperors. Tacitus suggests that the personal physician of Claudius may possibly have assisted in the poisoning of that emperor. By the time of Theodosius the word "medicamentarius" meant "poisoner," although earlier it had meant only "drug-seller." According to Herodian, the first act of Caracalla was to order the execution of the court physicians because they refused to hasten the death of his father Severus (Withington). The Romans, by the way, knew many poisons, some acting quickly in small quantities. Prussic acid had been extracted from the kernel of the peach by the Egyptians. The Assyrians knew aconite, mandragora, hemp, and several mineral poisons such as arsenic, antimony, and copper. Pliny and other Latin authors used the word "cicuta" when alluding to the state poison of the Greeks; combined with opium it makes a very potent poison even in small quantities. There are at least twenty-five varieties of poisonous mushrooms. (*Amanita phalloides*) and probably most of these were known to the Romans, who were capable of extracting the essential poison. Theophrastus states that the most subtle poison was aconite.

With the gradual organization of medical study, which we shall shortly discuss, the social position of the physician improved. In 46 B.C. Julius Caesar granted the rights of Roman citizenship to all physicians, which ensured an increased dignity

to the practice of medicine. This was probably brought about by the need for trained surgeons in the army, and may have been preliminary to the establishment of an army medical service. At the close of the first century A.D. the city garrison consisted of twenty cohorts, each provided with four surgeons; the thirty legions had from six to ten surgeons each; the infantry and cavalry of the allies probably had surgeons of an inferior class, and the stationary camps of the standing army would be supplied with camp surgeons. In spite of the right of citizenship, the practice of medicine continued to be regarded as unworthy of a Roman patrician. Cicero says that the practice of medicine is commendable "to those whose rank and condition is suitable for such employment." Many physicians, however, quickly acquired wealth, and with it adopted a luxurious mode of living. They were then often accepted into patrician society. The immigration of the mediocre physicians, seeking fortunes, gave place to the arrival of more illustrious practitioners who were attracted by the glories of the great city. The satirical poets, for the most part, had only contempt for physicians, but the more serious writers gradually came to look upon them as worthy persons. An example is Quintilian who proposed the following case for debate: a man having three sons, a philosopher, a physician, and an orator, divides his property into four parts, and leaves the extra share to the one most useful to the state; which son should have it?

The social status of the physician slowly improved by the influence of the learned and honest practitioners. According to Suetonius, during a famine in Rome in 46 B.C. Caesar ordered the expulsion of all foreigners except teachers and doctors. Augustus in 10 A.D. granted doctors immunity from taxes and from many public duties. Vespasian confirmed this privilege, and Hadrian published rules defining these immunities. Antonius Pius, however, ordained that the privileges should not apply to all doctors, but only to a certain number of them, in smaller towns five, in the middle-sized ones seven, and in larger ones ten. Later the immunities applied only to public medical officers.

Let us now glance at the subject of the medical education of the physician in Rome. As we have noted, the gradual organization of medical study played a part in changing the social status of the physician. As medical practice was almost entirely in the hands of the Greeks, the education of the physician was Greek education, at least until the time of the Empire. Scientific medicine began with the Greeks. The scientific method begins with careful, objective observation, uninfluenced by subjective beliefs. The results of the observations are accurately recorded and systematically classified. From the data a law or theory is evolved by inductive reasoning. So far the Greeks went, but they did not take the final step of experimental verification of the theory. The mythical Aesculapius, to whom Pindar refers as "the son of Apollo by the nymph Coronis," was worshipped as a deity, and his most celebrated temples were at Cos, Cnidus, Pergamus, and Epidaurus. These shrines became popular sanitaria controlled by priest-physicians. They have been described by Aristophanes in a facetious manner, and by Walter Pater more sympathetically. The votive tablets at these shrines became a sort of clinical record. Pausanias mentions six of them when he visited the temple of Epidaurus in 150 B.C. Two of them, excavated in modern times, have very meagre details of symptoms and treatment. Nevertheless they must have

been of value in the gradual understanding of the course of many diseases. In addition to the priest-physicians there were practitioners not attached to the Aesculapian shrines. Moreover, medicine was studied, along with philosophy and rhetoric, as part of the general education. It was practised in some of its details by the "Gymnasts." Osler has observed that, "Greek medicine had a triple relationship with science, with gymnastics, and with theology." Before the time of Hippocrates it was regarded simply as a branch of philosophy, and Pythagoras (580–548 B.C.) included medicine in his philosophical writings. The Greek physician, therefore, began with a good general education, and his study of medicine consisted of observation from which there was evolved a very accurate description of the clinical course of many diseases. This was carried out under the tutelage of a priest-physician, or of a private practitioner. Before practice he took an oath based upon the finest ethical principles. Therapy was not based on any philosophical system, and consisted mostly of regulation of diet, rest, and hydrotherapy. In Rome this was soon changed, and treatment became based upon some system of philosophy.

By the time of the Republic, Roman instruction seems to have been conducted privately, and without any state control, yet medicine formed part of the general culture, and Athenaeus maintained that every cultured man should concern himself with its study. The organization of medical study began with the granting of citizenship to the physicians by Julius Caesar, and this was a check upon the activities of ill-trained and pseudo-physicians.

In southern Italy and in Sicily medical schools developed adjacent to, and under the influence of, philosophical schools, and to these many students travelled for instruction. The college of the Archiatri, which we shall shortly describe, outlined a course of instruction, and the physician who completed it was called "Medicus a Republica." Many students did not complete the course, but, nevertheless, set up in practice. Galen estimated that at least eleven years' study was necessary for the education of a competent physician. His contemporary and enemy, Thessalus, declared that six months' study was sufficient to make an excellent physician. Many of the students of Thessalus, says Galen, could neither read nor speak correctly. The Romans never saw any usefulness in disinterested research. They collected previous writings and made encyclopaedias of science without ever trying to verify the opinions expressed. Towards the end of the Empire there was certainly public instruction in medicine, and by the time of Hadrian (331–6 A.D.) physicians had their place in the Athenaeum.

Just how a distinct medical class was brought about we do not know. Puschmann suggests that the necessity for skilled medical men in the army was a factor. Tacitus says that in more ancient times the soldiers carried bandages, and each took part in the care of the wounded. Livy states that, after the battle of Sutrium in 309 B.C., more soldiers died of wounds subsequently than were killed in battle, yet even at that time medicine was practised as a profession in Rome, as attested by the same author. It is rather interesting to note that, although anyone was free to practise medicine if he could obtain patients, yet, as Carcopino points out, barbers were not permitted to set up shop until they had completed

an adequate apprenticeship. Romans might trust their health, but not their faces, to the untrained.

A true organization of medical study in Rome dates from the commencement of the third century when Alexander Severus (225–35 A.D.) instituted special schools for the teaching of medicine, and granted stipends to the teachers and assigned them public lecture rooms. The study consisted of mammalian anatomy, the examination of wounds, medical botany, and some clinical instruction. The latter was often given in the house of the patient, about which Martial has to say,

> "Faint was I only, Symmachus, till thou,
> Backed by an hundred students, throng'dst at my bed;
> An hundred icy fingers chilled my brow.
> I had no fever; now I'm nearly dead."

At a later period the Archiatri, more than others, appear to have devoted themselves to the business of teaching. The duration of study depended upon the ability, desire, and wealth of the student. The art of medicine was more profitable, and less laborious to learn, than was its science, therefore men like Thessalus looked with contempt on the theoretical side of medicine. From the time of Galen anatomy became more and more important, but there was little interest in physiology. Materia medica was an important study, and Dioscorides, a Greek army surgeon in the service of Nero, was one of the greatest of the medical botanists. He listed about five hundred plants so accurately that most of them can be recognized today. Most doctors prepared their own medicines, and Pliny says that the ordinary public believed that the most expensive remedies were also the most potent for good. By the time of Galen medicine and surgery were separate subjects of education, and few doctors practised both. Celsus mentions many surgeons by name. The Roman surgeon of Galen's time had much sound knowledge, and performed even major operations requiring anatomical knowledge and technical skill. He had many surgical instruments; about an hundred of these have been recovered in the excavations at Pompeii. Celsus says that ligatures and torsion of vessels were used when simpler methods of arresting haemorrhage failed. Whether artificial limbs were in use is a question on which there is much argument, but Lucian refers to artificial feet made of figtree wood. A law, said to have been made by Numa Pompilius, ordained that Caesarean section should be performed on women dying in labour in order, if possible, to save the life of the child. Pliny says it was carried out also on living women, and that Scipio Africanus owed his life to this operation. There were some female doctors, and in one collection of epitaphs Carcopino found reference to four women physicians along with fifty-one men.

Although anyone was free to practise medicine in Rome without examination of his qualifications, yet for the public sanitary service, and for admission to the Archiatrate, examination was necessary. So, in practice, there was a distinction between trained and untrained doctors. Probably most of the specialists belonged to the latter group, as they were men who were unwilling to take the necessary training, or were incapable of mastering it. Today the specialist is a well-trained

physician who has added a long special training to his basic medical education.

There was a friendly relationship between the best physicians and surgeons, and consultation was common. The social position of the surgeon was not inferior to that of the physician, as it became later.

Prognosis, meaning a description of the course of a disease and its probable outcome, was of great importance to the Roman physician. There were two reasons for this. Little was known about efficient therapy, and the idea of suicide was not opprobrious. If, therefore, one were suffering from a painful disease that would probably end fatally, it was not shameful that he should take his own life at a moment and in a manner of his own choosing.

By the time of the Emperor Claudius (41–54 A.D.) the order of the Imperial Archiatri had arisen. The Archiatrate at one time was thought to be a purely Roman institution, but the office, as well as the name, appears to be Greek. Historians distinguish several classes of Archiatri, but are not agreed on the number. The Palatine Archiatri were court physicians, and public health and the care of the poor were assigned to the Archiatri Populares of five, seven, or ten communal physicians in each city, according to its size. About 378 A.D. an Archiater was appointed to each of the fourteen districts of Rome by the Emperor Valentinian. In addition, several physicians were designated for the Porticos, and for the College of Vestal Virgins. All of these physicians were under the control of the central government, and were elected by vote of the existing members of the Archiatri. Some of the court physicians received handsome salaries, but were debarred from private practice. The Archiatri Populares were permitted private practice, and instructed students, for a fee if the students were able to pay, gratis if they were not. At first ordinary physicians enjoyed almost equal privileges with the Archiatri, but later their rights were more circumscribed. The Palatine Archiatri played an important part in political life. The title—Archiater—was sometimes given to celebrated physicians who were not connected with the court or with the public medical service. The Society of Archiatri served as a model for the medical guilds of surgeons.

We may now consider briefly the outstanding writers and practitioners. We have seen that the influence of Asclepiades established Roman medicine on a firm foundation. Themison, who was one of his pupils, founded the school of the Methodists. Juvenal refers to him in derogatory terms. This school attempted to confine medicine to rigid doctrines, the basic one being that all disease comes from a state either of tension, or relaxation. It was found necessary later to introduce a third concept to explain symptoms, so the system eventually recognized "status strictus," "status laxus," and "status mixtus." Therapy consisted in combatting these states. The system is simple, lends itself to easy explanations, and, because of its simplicity, met with favour by the common people.

The licentiousness of Imperial Rome, with widespread immorality, and abnormal sexual practices among all ranks, would be expected to give rise to venereal diseases, although syphilis was probably unknown.

Gynaecology was one of the specialties practised in the Empire, and Soranus of Ephesus was the author of one of the most important treatises on obstetrics and the diseases of women written before modern times. It was the basis of

Roslin's *Rosengarten* published in 1513, and of Raynalde's *Byrthe of Mankynde* in 1545. Soranus instructed midwives to keep their fingernails trimmed, and to be circumspect in their bearing. He believed that the most favourable period for conception was just after a menstrual period, a belief which persisted until very recently. A three-bladed gynaecological speculum has been recovered in the ruins of Pompeii, which was destroyed in his time. The knowledge of this instrument was lost in the Middle Ages, and was rediscovered only in 1815. The chapter on the anatomy of the female pelvis is the most important one in Soranus' book.

The best we have of Roman medicine is the work of Celsus. He was one of the greatest of the Latin medical writers, but it is a matter of controversy whether he ever practiced medicine. The Loeb Library points out that it was not unusual for a Roman gentleman to have a fairly intimate knowledge of medicine, but its practice was looked upon as beneath his dignity. On the other hand, Celsus expresses his opinion as to the treatment of symptoms by using the first person of the verb, and often uses the emphatic "ego." Moreover, he writes of patients he knew personally, and attended even by night. He was classed by Pliny among the men of letters, and was ignored by contemporary practitioners, who thought that a Roman could not know much medicine. His is the oldest medical document after the Hippocratic writings, and, of the seventy-two medical authorities mentioned by him, only the work of Hippocrates has come down to us relatively intact. He was the first to translate Greek medical terms into Latin, and the nomenclature which he began still persists. He criticized both the Empiricists, who pretended to cure all diseases by means of drugs, and the Methodists who supposedly cured them all by diet and exercise. An indication that dissection was allowed in Rome at that time is seen in his statement, "To open the bodies of the dead is necessary to learners." He distinguished accurately between the quotidian, tertian, and quartan fevers of malaria. His work was the first attempt at a history of medicine.

Pliny the Elder (23–79 A.D.) was not a physician, but Books 20 to 32 of his *Natural History* deal exclusively with medicine. There are references to scurvy, superfoetation, and even to the possible use of an eye-glass by Nero. He says, "Nero princeps gladiatorum pugnas spectabit in smaragdo." Smaragdus, of course, means an emerald, and it is possible that he was gazing through some mineral which might have been ground to magnify. Neuberger notes that reading a passage in Pliny about the use of the juice, anagallis, before operating for cataract gave Himly the idea of investigating the action of belladonna on the pupil.

The greatest of the Latin physicians and writers was Galen (131–200 A.D.) who retained the position of medical dictator of the western world for a thousand years. His medical hypotheses were based upon the philosophy of Aristotle, were acceptable to the Church, and hence remained unassailable for centuries. He was the son of an architect, and had studied philosophy until the age of twenty, when his medical education began. It is the opinion of Baas that Galen was more of a savant and teacher than practitioner, but we know that his practice was extensive and excellent. He was an investigator with a true scientific spirit.

His chief physiological work was the investigation of the nervous system, and he distinguished sensory, motor, and mixed nerves. He produced hemiplegia by section of the spinal cord, and aphonia by cutting the recurrent laryngeal nerves. His first court case was the cure of Marcus Aurelius of a stomach-ache due to eating too much cheese. His knowledge of anatomy in a celebrated case led him to diagnose a lesion of the spinal cord in a patient who had sensory paralysis of one half of his hand. There are several interesting stories of his astuteness. One concerns a lady with an ill-defined disability and no symptoms. With his finger on her pulse he engaged her in conversation, during which he made casual mention of a popular actor named Pylades, and her pulse immediately accelerated. He repeated his observation on another day, and arrived at the correct diagnosis of "love-sickness." Hippocrates had separated medicine from philosophy; the aim of Galen was to unite them.

There are many sidelights on Roman medicine by non-medical writers. Plautus and Terence have several references to obstetrics. Lucretius refers to anatomy, physiology, and dietetics, as well as giving us the famous account of the plague in Rome. Ovid, Tibullus, and Propertius refer to sexual vices, venereal disease, aphrodisiacs, and cosmetics. Virgil described anthrax in sheep. Mosquito netting (*conopium*) is mentioned by Horace and Juvenal.

Should we attribute to Roman civilization a decisive effect upon the progress of medical science, or should we regard Roman medicine as essentially Greek medicine? Most recent historians are of the latter opinion. It should be remembered, however, that if scientific medicine made little progress in Rome, it was there that the rules of hygiene were codified, and legal medicine had its beginning. Rome devised excellent sanitation and water supplies, organized medical care of the poor, and medical services for the armed forces. Scientific and theoretical medicine deteriorated, but practical and technical medicine advanced. The work of the encyclopaedists has preserved for us some of the contents of texts which disappeared in antiquity. The productive genius of the Greeks was lacking for the Romans were deficient in creative imagination, yet, under them, surgery, including obstetrics and ophthalmology, attained a degree of excellence which it was not to reach again before the sixteenth century.

NEWS LETTER

Midwinter Council Meeting

The regular midwinter meeting of the Council of the Canadian Anaesthetists' Society was held in Toronto on Sunday, March 6, 1955. The Council met from 10 A.M. to 6.45 P.M. All Divisions were represented except Prince Edward Island and Newfoundland.

The Council considered and approved the Financial Statements for 1954, and after careful consideration of the budget for 1955 recommended that the General Meeting in June should be asked to increase the membership fee in each class by $5.00. Thirty-five applications for membership were approved for forwarding to the general meeting of the Society. It was agreed that the Canadian Anaesthetists' Society Tariff of Fees should be revised, and directed that the details should be decided at the June meetings of Council.

Council accepted the financial responsibilities implicit in membership in the World Federation of Societies of Anaesthesiologists, and appointed Dr. H. R. Griffith, Dr. R. A. Gordon, and Dr. S. M. Campbell as delegates to the organizational meeting in Holland in September, 1955.

Western Canada Regional Meeting

The four Western Divisions of the Canadian Anaesthetists' Society held their tenth annual regional meeting in Regina on April 21 to 23, under the auspices of the Saskatchewan Division. The meeting was an outstanding success, and great credit is due to the Executive of the Saskatchewan Division, of which Dr. M. W. Bowering is Chairman and Dr. Trevor Darke Secretary-Treasurer, to Dr. J. E. McCutcheon, who was responsible for programme, and to the commercial exhibitors. Guest speakers were Dr. R. G. B. Gilbert, Montreal; Dr. R. A. Gordon, Toronto; Dr. E. Ring, Regina; and Dr. J. E. Merriman, Saskatoon. Western Canadian anaesthetists contributing to the programme were Dr. Angus MacMillan and Dr. Jone Chang, Vancouver; Dr. S. G. Paletz, Edmonton; Dr. Gordon Wyant and Dr. Vyvian Morton, Saskatoon; Dr. Donalda Huggins and Dr. John Davies, Winnipeg; Dr. D. McAlpine and Dr. M. W. Bowering, Regina; Dr. D. M. Ewart, Moose Jaw. Dr. and Mrs. Bowering kindly loaned their home for an evening reception by the Saskatchewan Division, and the meeting was concluded by an enjoyable cocktail party and dinner dance at the Hotel Saskatchewan.

On invitation of the British Columbia Division, the next Western regional meeting will be held in Vancouver, B.C., during the second week of March, 1956.

Manitoba Division Meeting

The Manitoba Division of the Canadian Anaesthetists' Society held a meeting at the Grace Hospital, Winnipeg, on April 20, 1955. Dr. R. A. Gordon of Toronto discussed "Chlorpromazine" and Dr. R. G. Gilbert of Montreal "The Care of Respiration." The speakers were the guests of the Manitoba Division at dinner following the meeting.

Dr. John Gillies Addresses the Toronto Academy

Anaesthetists from Western, Central, and Eastern Ontario were invited by the Section of Anaesthesia, Toronto Academy of Medicine, to be present at a recent dinner in honor of Dr. John Gillies, Sir James Y. Simpson Reader in Anaesthesia at Edinburgh University.

Later in the evening, Dr. Gillies addressed a large and interested audience in Osler Hall at the Toronto Academy. His subject was "Induced Hypotension."

The speaker mentioned the advantages of hypotension produced by Spinal anaesthesia and ganglioplegic drugs. He mentioned several points that were particularly interesting to his audience:

1. A level of 70 mm. Hg. is safe. Prompt replacement of blood loss is necessary and proper posture is important to avoid embarrassment of cerebral circulation.
2. Carefully supervised hypotension produced by these methods in experienced hands resulted in an incidence of complications that was no higher than occurred in larger series of similar cases where no hypotension was used.
3. When general anaesthesia is used variations in depth of anaesthesia may result in a variation in the hypotension. This variability is not present when there is an associated sensory block as occurs in methods induced by Spinal anaesthesia.
4. The decrease in blood replacement requirements associated with these methods may well be of great advantage in the event of a future national emergency, when a scarcity of whole blood for transfusion purposes will be inevitable.
5. Occasional episodes of prolonged hypotension occur with Arfonad.
6. Renal plasma flow is not decreased.

Dr. Gillies answered many questions for us. He clarified and explained many of the controversial points. After having received the benefit of his great experience with the method, we were profoundly thankful for his instruction and advice.

*

Dr. Allen B. Dobkin has been appointed Assistant Professor of Anaesthesia at the University of Saskatchewan, effective July 1, 1955. Dr. Dobkin has recently been Senior Instructor in Anesthesiology at Western Reserve University, Cleveland, Ohio.

Dr. Ann B. Henschel has been appointed Clinical Associate in the Department of Anaesthesia of the University of Saskatchewan.

*

Dr. H. Barrie Fairley, F.F.A.R.C.S., has been appointed a Clinical Assistant in the Department of Anaesthesia, Faculty of Medicine, University of Toronto, and the Department of Anaesthesia, Toronto General Hospital, and has joined Anaesthesia Associates of Toronto in the private practice of anaesthesia. Dr. Fairley was recently Senior Anaesthetics Registrar at the Brompton Hospital, London, England.

BRONCHIAL OBSTRUCTION BY REGURGITATED BLOOD: A CASE REPORT

THE patient, a 30-year-old male, was admitted to hospital February 3, 1955, and three days later became icteric. Infectious hepatitis was diagnosed. On February 10 persistent gastro-intestinal haemorrhage developed with frequent bloody stools. A diagnosis of bleeding duodenal ulceration was made February 14 and the decision to perform a partial gastrectomy was made with the onset of the third major haemorrhage on February 17.

He was transfused preoperatively and came to the operating room in good condition. Anaesthesia was accomplished with endotracheal cyclopropane following pentothal induction. This was supplemented by a 0.2 per cent succinylcholine chloride drip throughout the four and a half hour procedure.

The immediate postoperative course was stormy. An intranasal Levin tube for continuous gastric suction functioned well but was poorly tolerated. Co-operation by the patient was poor. Chest exercises and coughing up of mucus were inadequately performed. Air entry was much reduced in both lung bases by the morning of the second postoperative day—temperature 99.4, pulse 120, respiration 30, colour normal. It was decided to initiate Alevaire inhalation therapy and to further encourage coughing efforts as much as possible.

While starting this treatment, the patient coughed, gagged, and vomited 6 to 10 oz. of bright red blood and blood-clots. His condition deteriorated suddenly. He appeared to choke and became cyanosed. He was turned on his right side to facilitate the clearing of his mouth and pharynx. Oxygen was administered by mask with prompt improvement in colour but respiration was so embarrassed as to require continual oxygen therapy. Air entry was further reduced in the right chest following this episode. Respiration and pulse were very rapid.

Two hours after the onset of this incident the patient was seen by one of us. Respiration was still rapid and oxygen by B.L.B. mask was needed to maintain normal colour. Air entry was much reduced, particularly to the right base which was dull to percussion. The mediastinum was deviated to the right in the chest film. During the examination, the patient coughed and produced a large clotted blood cast of the trachea. It was now obvious that there was blood in this man's tracheo-bronchial tree but its source was in doubt. It could have risen from a tracheal ulceration or from "silent" aspiration of regurgitated blood. Immediate bronchoscopy under topical anaesthesia was decided upon.

As the trachea was entered a great quantity of blood was immediately expelled with explosive violence. The right main bronchus was found to contain much blood which was removed by suction. The left bronchial tree was essentially clear. No ulceration of the trachea or other local source of bleeding was discernible.

Following bronchoscopy, the patient was definitely improved. Respiration and pulse continued rapid. Colour was normal without oxygen. He was, nonetheless, placed in an oxygen tent with nebulized Alveaire.

During the next 48 hours, the patient's condition steadily improved. His further course was complicated, not unexpectedly, by an abdominal dehiscence on the sixteenth postoperative day. Following the reparative operation, a bronchopneumonia developed which cleared slowly. From then on, he convalesced uneventfully.

We can speculate as to whether this aspiration occurred gradually over a period of time or whether it followed the episode of vomiting. We favour the latter explanation.

We think it unusual that a postoperative patient with a functioning Levin tube in place should silently aspirate sufficient regurgitated blood to produce complete filling and obstruction of the right main bronchus.

L. H. E.

Kingston, Ont.

BOOK REVIEWS

LOCAL ANALGESIA: BRACHIAL PLEXUS. By R. R. MACINTOSH (Nuffield Professor of Anaesthetics, University of Oxford) and WILLIAM W. MUSHIN (Professor of Anaesthetics, Welsh National School of Medicine, University of Wales). Third ed., Edinburgh and London: E. & S. Livingstone Ltd. [Macmillan Company of Canada Limited]. 1954. Pp. 62, 43 illus. $1.80.

The third edition of this excellent book, published in 1954, is now available. There are very few changes over the previous second edition of 1947. The section on local anaesthetic solutions recommends the use of Xylocaine as a local anaesthetic agent, and also of Hyaluronidase in anaesthetic solutions. The section on the Stellate Ganglion has been enlarged slightly and is a little more descriptive. The section on Complications has included, briefly, the treatment of pneumothorax.

This concise, excellently illustrated treatise on Brachial Plexus Block Anesthesia should be seen on the shelf of every anaesthesiologist or medical practitioner who is practising anaesthesia. It is one of the best books available in medical literature today.

H. B. GRAVES

BASIC SCIENCES IN ANESTHESIOLOGY: A GUIDE FOR STUDY. By ARTHUR B. TARROW (Lt. Col., United States Air Force (Medical Corps)). 2nd ed., San Antonio, Texas: Lydette Publishing Company. $5.00.

This volume covers the subjects of Anatomy, Physiology, Pathology, Physics and Chemistry, and Pharmacology. The material is arranged in question and answer form, and each answer is referred to a standard text-book source. The questions are in the "true or false" form current with the examinations of the American Board of Anesthesiology, and although this reviewer has, personally, no use for this type of question, it is undoubtedly true that Col. Tarrow's volume will be of great value as a guide to those reviewing their knowledge of the basic sciences for the Board examinations.

R. A. GORDON

LOCAL ANALGESIA: ABDOMINAL SURGERY. By R. R. MACINTOSH and R. BRYCE-SMITH. Edinburgh and London: E. & S. Livingstone Ltd. [Macmillan Company of Canada Limited]. $1.80.

The widespread use of curare and other relaxants has greatly reduced the indications for regional anaesthetic techniques in abdominal surgery. However, these procedures are still of value, particularly for those cases in which the hazards of anaesthesia may be increased by the use of a relaxing agent, e.g. bowel obstruction or strangulated hernia.

In this small volume—and its size is one of the best features, since it is much more likely to be read thoroughly than if it were a large tome—the authors have presented, clearly and concisely, the nerve block techniques which may be used

for abdominal surgery of all types. Some are well-known techniques, others are new in their approach.

One refreshing feature of the book, also found in others from the same centre, deserves special mention. The authors obviously assume that their work will be read by those of at least average intelligence. The book is readable and the "instruction by numbers" presentation so often found in books on regional anaesthesia is carefully avoided.

Each section of the text is fully illustrated with diagrams and drawings which by their clarity and by proper positioning in relation to the text illustrated, enhance greatly the usefulness of the book.

I. M. MACKAY

ELEMENTS OF PEDIATRIC ANESTHESIA. By C. R. STEPHEN, B.SC., M.D.C.M., D.A. Toronto: Ryerson Press. $4.00.

The need for an up-to-date book dealing with recently developed drugs and current techniques used in paediatric anaesthesia is generally recognized. The monograph under review unfortunately fails to fill this gap in our literature. Dr. Wesley Bourne in his foreword states "In his [the author's] diction nothing is oblique and one finds relevancy everywhere." Unfortunately we cannot share this opinion.

The first third of the book is devoted to a description of the physiological peculiarities of smaller children as they relate to anaesthesia. The basic principles outlined in this section are sound, holding true for any age group or anaesthetic technique, although some of them are relatively more important in paediatric work. Some of the details here are rather puzzling, however, for example the recommendation that ¼ to ⅕ isotonic saline be administered by vein.

The chapter on anaesthesia in premature infants might well have been expanded beyond the single page devoted to this difficult group.

The chapter entitled the "Thymic Child" is confusing, in that while the thymus gland is exonerated as a cause of sudden death a "thymic" syndrome is described. Surely this ghost was laid years ago.

The succeeding chapters deal in turn with premedication, basal anaesthesia, techniques, clinical pharmacology of anaesthetic drugs, and choice of anaesthesia for various specific operations. The book concludes with a description of oxygen therapy techniques and the treatment of asphyxia neonatorum. The criticism of these chapters is that an attempt has been made to cover far too much in far too little space, with the result that nothing is really covered adequately. An example is the section entitled "Curariform Drugs" in which only curare itself is mentioned to the complete exclusion of all curariform agents as well as the depolarizing relaxants now in widespread use.

The conception of the section on the physiology of infants as related to anaesthesia has much merit. We would like to see this portion expanded into a full monograph which would be a worth-while contribution to the literature. It is unfortunate that with all of the knowledge at his disposal and his broad experience in the paediatric field the author has not produced a better book.

CODE SMITH

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References:

1) C. Thelen, **Jackson Clin. Bulletin 12**:119, 1950.
2) W. M. Kane, **Am. J. Obst. & Gynec., 65**:1020, 1953.
3) L. E. McCrea and E. Post, **J. of Internat. College of Surgeons, 21**:4, 1954.
4) H. W. Gierson, L. S. Gottlieb, H. J. Rubin, **Dis. of the Chest, 27**:1, Jan. 1955.

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INDEX OF ADVERTISERS

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References to the literature should be clearly indicated in the text by arabic numerals in brackets, thus (4). They should be set out in numerical order at the end of the article, typed in double space, as follows:

4. Griffith, H. R. & Johnston, G. E. The Use of Curare in General Anaesthesia. Anesthesiology *3*: 481 (1942).

References to books will state in order: Name of Author, Title of Book, Edition, Place of publication, Publisher, Year of Publication, such as:

Labat, G. Regional Anesthesia. 1st ed., Philadelphia: Saunders (1922).

The names of all authors will be given in the first instance in each reference. In further references to the same authors the abbreviated form "Griffith *et al.*" may be used.

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CONTENTS

VOL. 2, NO. 3 JULY, 1955